201-15166B

# Appendix I

# Benzyl Mercaptan

# I U C L I D

# Data Set



| | | |
|---|---|---|
| **Existing Chemical** | : | ID: 100-53-8 |
| **CAS No.** | : | 100-53-8 |
| **EINECS Name** | : | toluene-alpha-thiol |
| **EINECS No.** | : | 202-862-5 |
| **Molecular Formula** | : | C7H8S |
| **Producer Related Part** | | |
| **Company** | : | Chevron Phillips Chemical Company LP |
| **Creation date** | : | 24.11.2003 |
| **Substance Related Part** | | |
| **Company** | : | Chevron Phillips Chemical Company LP |
| **Creation date** | : | 24.11.2003 |
| **Memo** | : | |
| **Printing date** | : | 06.01.2004 |
| **Revision date** | : | |
| **Date of last Update** | : | 06.01.2004 |
| **Number of Pages** | : | 63 |
| **Chapter (profile)** | : | Chapter: 1, 2, 3, 4, 5, 7 |
| **Reliability (profile)** | : | Reliability: without reliability, 1, 2, 3, 4 |
| **Flags (profile)** | : | Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS |

### 1.0.1 OECD AND COMPANY INFORMATION


**Type** : other
**Name** : Chevron Phillips Chemical Company LP
**Partner** :
**Date** :
**Street** : 10001 Six Pines Drive
**Town** : 77380 The Woodlands, TX
**Country** : United States
**Phone** :
**Telefax** :
**Telex** :
**Cedex** :
24.11.2003


### 1.2 SYNONYMS

(Mercaptomethyl) benzene
24.11.2003

alpha-Toluenethiol
24.11.2003

alpha-Tolyl mercaptan
05.12.2003

Benzyl mercaptan
24.11.2003

Benzylhydrosulfide
24.11.2003

Benzylthiol
24.11.2003

Phenylmethanethiol
24.11.2003

Phenylmethyl mercaptan
24.11.2003

Thiobenzyl alcohol
24.11.2003

## 2.1 MELTING POINT

| | | |
|---|---|---|
| **Value** | : | = -30 ° C |
| **Sublimation** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Remarks** | | Selected Melting Point (calculated mean value) was -19.22 ºC. |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | MPBPWIN (v 1.40) Experimental Melting Point |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (14)

## 2.2 BOILING POINT

| | | |
|---|---|---|
| **Value** | : | = 194 - 195 ° C |
| **Decomposition** | : | |
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | Patty's Industrial Hygiene and Toxicology (Bingham, 2001). |
| **Test substance** | : | Benzyl Mercaptan (CAS Number 100-53-8), purity not given |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (2)

| | | |
|---|---|---|
| **Value** | : | = 194 - 195 ° C |
| **Decomposition** | : | |
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | The Merck Index (O'Neil, M.J., 13th ed.) |
| **Test substance** | : | Benzyl mercaptan (Thiobenzyl Alcohol) CAS Number 100-53-8, purity not given |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

26.11.2003 (13)

| | | |
|---|---|---|
| **Value** | : | = 194.5 ° C |
| **Decomposition** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | MPBPWIN (v 1.40) Experimental Boiling Point |
| **Remarks** | | The Boiling Point was calculated to be 200.14 ºC using the Adapted Stein & Brown Method. |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (14)

## 2.4 VAPOUR PRESSURE

| | | |
|---|---|---|
| **Value** | : | = 0.632 hPa at 25° C |
| **Decomposition** | : | |
| **Method** | | other (calculated): EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | EPIWIN Selected Vapor Pressure (Mean of Antoine & Grain methods). Vapor Pressure Estimations (25 deg C) using BP: 194.50 deg C. |
| **Result** | : | 0.474 mm Hg (0.632 hPa) at 25 deg C. |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

31.12.2003 (14)

## 2.5 PARTITION COEFFICIENT

| | | |
|---|---|---|
| **Log pow** | : | = 2.48 |
| **Method** | | other (calculated): EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | WSKOW v 1.40, EPIWIN v 3.10. |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

26.11.2003 (14)

## 2.6.1 WATER SOLUBILITY

| | | |
|---|---|---|
| **Value** | : | = 732.2 mg/l at 25 ° C |
| **Qualitative** | : | moderately soluble (100-1000 mg/L) |
| **Pka** | : | |
| **PH** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | Water Solubility calculated from Kow (WSKOW v1.40). |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

31.12.2003 (14)

### 3.1.1 PHOTODEGRADATION

| | | |
|---|---|---|
| **Type** | : | other |
| **Light source** | : | |
| **Light spect.** | : | |
| **Rel. intensity** | : | |
| **Deg. Product** | : | |
| **Method** | : | other (calculated): EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | Calculated using EPIWIN v 3.10, AOP Program v 1.90. |
| **Result** | : | Overall OH Rate Constant = 44.6303 E-12 cm3/molecule-sec<br>Half-Life = 0.240 Days (12-hr day; 1.5E6 OH/cm3)<br>Half-Life = 2.876 Hrs |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

31.12.2003 (14)

### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

| | | |
|---|---|---|
| **Type** | : | fugacity model level III |
| **Media** | : | other: air-water-soil-sediment |
| **Air (level I)** | : | |
| **Water (level I)** | : | |
| **Soil (level I)** | : | |
| **Biota (level II / III)** | : | |
| **Soil (level II / III)** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **Method** | : | Used EPIWIN v 3.10. The following physical properties were used as the model input parameters:<br>Chem Name: Benzenemethanethiol<br>Molecular Wt: 124.2<br>Henry's LC: 0.000211 atm-m3/mole (Henrywin program)<br>Vapor Press: 0.474 mm Hg (Mpbpwin program)<br>Log Kow: 2.48 (Kowwin program)<br>Soil Koc: 124 (calc by model) |
| **Result** | : | Results are provided in the following format:<br>Compartment / 100% to Air / 100% to Water / 100% to Soil / Equally to Each Compartment<br><br>Air / 92.6% / 0.873% / 0.22% / 1.54%<br>Water / 6.13% / 98.6% / 1.85% / 36.0%<br>Soil / 1.2% / 0.011% / 97.9% / 62.3%<br>Sediment / 0.03% / 0.51% / 0.0096% / 0.19%<br><br>Air: half life = 5.75 hr; emissions = 1000 kg/hr |

Water: half life = 360 hr; emissions = 1000 kg/hr
Soil: half life = 360 hr; emissions = 1000 kg/hr
Sediment: half life = 1.44E+3 hr; emissions = 0 kg/hr

Persistence when distributed equally to each compartment = 235 hr
(Emissions (kg/hr) = 1000 to air, 1000 to water, 1000 to soil, and 0 to sediment)

**Source** : EPI Suite v 3.10.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
26.11.2003 (14)

## 3.5 BIODEGRADATION

**Type** : aerobic
**Inoculum** :
**Contact time** :
**Degradation** : = 40.7% after 28 days
**Result** : other: not readily biodegradable.
**Kinetic of test substance** :
7 day = 2.8**%**
15 day = 0.8**%**
21 day = 5.5**%**
28 day = 40.7**%**

**Control substance** : Benzoic acid, sodium salt
**Kinetic** : 7 day > 100**%**
28 day > 100**%**
**Deg. Product** : not measured
**Method** : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
**Year** : 1992
**GLP** : no data
**Test substance** : other TS

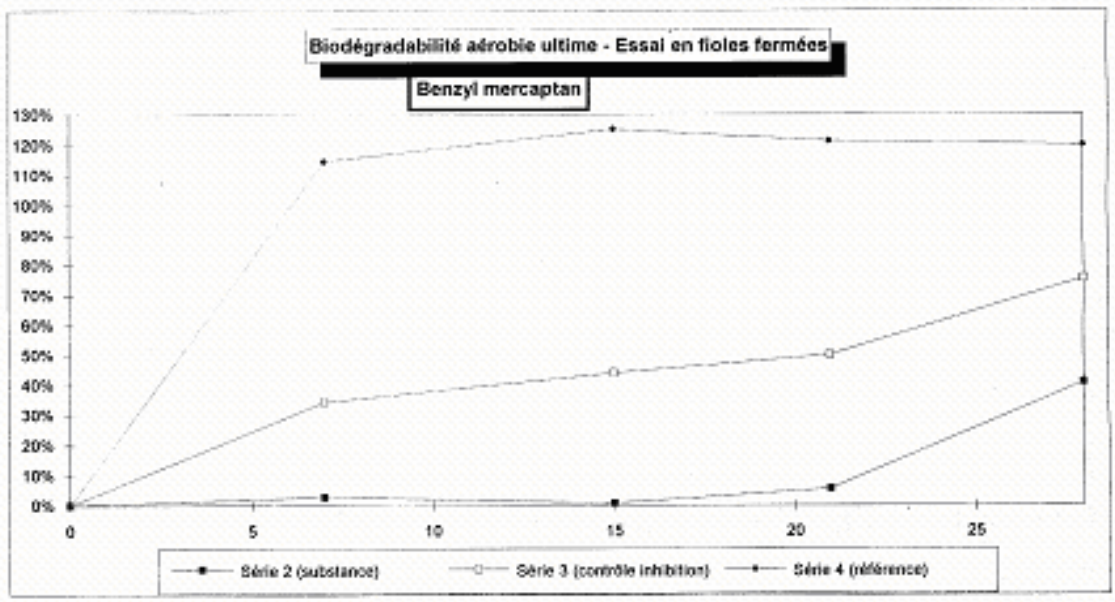
**Source** : ATOFINA, PARIS-PARIS-LA-DEFENSE, FRANCE

**Test condition** : DURATION OF THE TEST: 28 days
ANALYTICAL PARAMETER: The bacterial activity is evaluated by the consumption of dissolved O2, and the degradation follows from the difference between its consumption in flasks containing test substance and check flasks.
SAMPLING: 7, 15, 21, 28 days.

**Test substance** : Benzyl Mercaptan, CAS# 100-53-8, purity not given

**Attached doc.** : Courbe Benzyl mercaptan.bmp
Tableaux resultats Benzyl mercaptan.bmp

4353C4E.XLS Graphique 2

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4353C4E.XLS

**BIODÉGRADABILITÉ "FACILE"**
**ESSAI EN FIOLES FERMÉES**
Directive CEE 92/69 : C.4-E - Ligne Directrice OCDE 301 D

| | | | |
|---|---|---|---|
| SUBSTANCE D'ESSAI : | **Benzyl mercaptan** | N°CAL : | 4353/96 |
| Substance de référence : | Benzoate de sodium | | |

**MESURES DE L'OXYGÈNE DISSOUS**

| Série | Fiole | Temps (j) 0 | 7 | 15 | 21 | 28 |
|---|---|---|---|---|---|---|
| **1 - Milieu + inoculum** | | | | | | |
| | 1 | 8,8 | 8,5 | 8,3 | 8,1 | 8,0 |
| | 2 | 8,8 | 8,6 | 8,4 | 8,1 | 8,0 |
| | Moyenne | 8,8 | 8,6 | 8,4 | 8,1 | 8,0 |
| **2 - Milieu + inoculum + substance d'essai** | | | | | | |
| | 1 | 8,5 | 8,1 | 8,1 | 7,9 | 5,0 |
| | 2 | 8,5 | 8,1 | 7,9 | 7,8 | 4,9 |
| | 3 | 8,5 | 8,0 | 8,0 | 6,6 | 5,1 |
| | Moyenne | 8,5 | 8,1 | 8,0 | 7,4 | 5,0 |
| **3 - Milieu + inoculum + substance d'essai + substance de référence** | | | | | | |
| | 1 | 8,7 | 6,5 | 5,1 | 3,9 | 2,6 |
| | 2 | 8,6 | 5,7 | 5,4 | 5,3 | 3,0 |
| | Moyenne | 8,7 | 6,1 | 5,3 | 4,6 | 2,8 |
| **4 - Milieu + inoculum + substance de référence** | | | | | | |
| | 1 | 8,8 | 0,9 | 0,0 | 0,0 | 0,0 |
| | 2 | 8,8 | 0,9 | 0,0 | 0,0 | 0,0 |
| | Moyenne | 8,8 | 0,9 | 0,0 | 0,0 | 0,0 |

| | DCO ou DThO (mgO2/mg) | Concentration (mg/l) Série 2 | Série 3 | Série 4 |
|---|---|---|---|---|
| Benzyl mercaptan | 2,71 | 2,45 | 1,24 | |
| Benzoate de sodium | 1,67 | | 2 | 4 |
| Série 3 | 2,07 | | | |

**DBO spécifique (mg d'oxygène consommé par mg de substance)**

| Temps (j) : | 0 | 7 | 15 | 21 | 28 |
|---|---|---|---|---|---|
| Série 2 (substance) | 0,00 | 0,07 | 0,02 | 0,15 | 1,10 |
| Série 3 (contrôle inhibition) | 0,00 | 0,71 | 0,91 | 1,03 | 1,56 |
| Série 4 (référence) | 0,00 | 1,91 | 2,09 | 2,03 | 2,00 |

**BIODÉGRADATION (moyenne des fioles)**

| Temps (j) : | 0 | 7 | 15 | 21 | 28 |
|---|---|---|---|---|---|
| Série 2 (substance) | 0% | 2,8% | 0,8% | 5,5% | 40,7% |
| Série 3 (contrôle inhibition) | 0% | 34,3% | 44,0% | 50,0% | 75,4% |
| Série 4 (référence) | 0% | 114,5% | 125,0% | 121,3% | 119,8% |

**CLAUSES DE VALIDITÉ DE L'ESSAI**

| | |
|---|---|
| Consommation d'oxygène dans la série 1 < 1,5 mg/l à 28 jours : | oui |
| Concentration résiduelle dans les séries d'essais > 0,5 mg/l : | oui |

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**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
06.01.2004 (3)

## 3.7 BIOACCUMULATION

| | | |
|---|---|---|
| **BCF** | : | 16.32 |
| **Elimination** | : | |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | Calculated using BCF Program (v 2.14) |
| **Remark** | : | Estimated Log BCF = 1.213<br><br>Estimated Koc = 518 (using PCKOC Program [v 1.66]) |
| **Source** | : | EPI Suite v 3.10. |
| **Reliability** | : | (2) valid with restrictions |

31.12.2003 (14)

## 4.1 ACUTE/PROLONGED TOXICITY TO FISH

| | | |
|---|---|---|
| **Type** | : | other: ECOSAR Predicted LC50 |
| **Species** | : | other: Fish |
| **Exposure period** | : | 14 days |
| **Unit** | : | mg/l |
| **Analytical monitoring** | : | |
| **LC50** | : | c = 63.687 |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : ECOSAR Program (v 0.99g).

The following physical parameters were used:
Molecular Weight: 124.2
Log Kow: 2.48 (KowWin estimate)
Water Solubility: 178.9 mg/L (calculated)

**Result** : ECOSAR Class: Neutral Organic SAR (Baseline Toxicity)
Organism: Fish
Duration: 14-day
LC50: 63.687 mg/L (ppm)

**Source** : EPI Suite v 3.10.

**Test substance** : Benzenemethanethiol (CAS Number 100-53-8)

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (14)

| | | |
|---|---|---|
| **Type** | : | other: ECOSAR Predicted LC50 |
| **Species** | : | other: Fish |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **Analytical monitoring** | : | |
| **LC50** | : | c = 0.92 |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : ECOSAR Program (v 0.99g).

The following physical parameters were used:
Molecular Weight: 124.2
Log Kow: 2.48 (KowWin estimate)
Water Solubility: 178.9 mg/L (calculated)

**Result** : ECOSAR Class: Thiols (mercaptans)
Organism: Fish
Duration: 96-hr
LC50: 0.920 mg/L (ppm)

**Source** : EPI Suite v 3.10.

**Test substance** : Benzenemethanethiol (CAS Number 100-53-8)

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (14)

## 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

**Type** : static
**Species** : Daphnia magna (Crustacea)
**Exposure period** : 48 hour(s)
**Unit** : mg/l
**Analytical monitoring** : yes
**EC50** : c = 0.15
**EC50, 24h** : c = 0.26
**Method** : OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
**Year** : 1984
**GLP** : yes
**Test substance** : other TS

**Result** : RESULTS: EXPOSED
- Nominal/measured concentrations: Attached document.
- Effect data (Immobilisation): Attached document.

RESULTS: TEST WITH REFERENCE SUBSTANCE: The sensibility of the biologic reactive is controlled by a toxicity test with Potassium dichromate periodically.
- Concentrations: EC50/24h = 0.94 mg/l.

**Source** : ATOFINA, PARIS-PARIS-LA-DEFENSE, FRANCE

**Test condition** : TEST ORGANISMS
- Strain: Daphnia magna (crustacea) straus strain 5 or strain A.
- Source/supplier: Breeding colony was realized in the laboratory, organisms were selected by sieving.
- Breeding method: Not available.
- Age: Less than 24 hours.
- Feeding: Microscopic algae Raphidocelis subcapitata.
- Pretreatment: No.
- Feeding during test: No.
- Control group: Yes.

STOCK AND TEST SOLUTION AND THEIR PREPARATION
- Dispersion: No.
- Vehicle, solvent: No.
- Concentration of vehicle/ solvent: None.
- Other procedures: 100 mg of the substance were introduced in 1 litre of dilution water, stirred at 20°C during 24 hours. Daphnids were exposed to a concentration range of 0.08 to 8.45 mg/l forming a geometric progression with a factor of 1.8.

STABILITY OF THE TEST CHEMICAL SOLUTIONS: The concentrations had been maintained to within 80% of the initial concentration throughout the duration of the test.
REFERENCE SUBSTANCE: Potassium dichromate.
DILUTION WATER: was prepared in the laboratory using pure water and salts according to ISO 6341.
For one litre: 25 ml of the below solutions
1- 11.76g $CaCl_2, 2H_2O$/l ultrapure water.
2- 4.93g $MgSO_4, 7H_2O$/l ultrapure water.
3- 2.59g $NaHCO_3$/l ultrapure water.
4- 0.23g KCl/l ultrapure water.
- Aeration: aerated up until oxygen saturation.
- Ca/Mg ratio: 4.

- Na/K ratio: 10.
TEST SYSTEM
- Concentrations: Attached document.
- Renewal of test solution: No.
- Exposure vessel type: 120 ml closed flasks (as test glassware) were entirely filled with test solutions and closed with butyl rubber caps covered with PTFE.
- Number of replicates, individuals per replicate: 4 replicates and 5 daphnids by replicate.
- Test temperature: 19.5-20.5°C.
- Dissolved oxygen: > 2 mg/l.
- pH: 7.97-8.17.
- Adjustment of pH: No.
- Photoperiod: Incubation of test flasks in darkness.
DURATION OF THE TEST: 24 and 48 hours.
TEST PARAMETER: The percentage of daphnids immobilisation after 24 and 48 hours.
SAMPLING: 24, 48 hours.
MONITORING OF TEST SUBSTANCE CONCENTRATION: CPG.

**Test substance** : Benzyl Mercaptan, CAS# 100-53-8, 99.45% pure.

**Attached doc.** : Benzylmercaptan.bmp
Summary Benzylmercaptan.bmp

**Elf Atochem S. A.**
**Centre d'Application de Levallois**

| Concentration | | | | Immobilisation | |
|---|---|---|---|---|---|
| Nominale | Calculée | | | | |
| vol. solution. saturée (%) | Initiale (mg/l) | Finale (mg/l) | Final/Initial % | à 24 h (%) | à 48 h (%) |
| 10 | 8.45 | 8.08 | 96 | 100 | 100 |
| 5.56 | 4.69 | 4.49 | 96 | 100 | 100 |
| 3.09 | 2.61 | 2.50 | 96 | 75 | 100 |
| 1.71 | 1.45 | 1.39 | 96 | 75 | 100 |
| 0.95 | 0.80 | 0.77 | 96 | 80 | 100 |
| 0.53 | 0.45 | 0.43 | 96 | 75 | 100 |
| 0.29 | 0.25 | 0.24 | 96 | 55 | 85 |
| 0.16 | 0.14 | 0.13 | 93 | 25 | 15 |
| 0.09 | 0.08 | 0.07 | 88 | 25 | 20 |
| 0 | 0 | 0 | / | 5 | 0 |

Les bulletins d'analyses sont joints en annexe 4.

Les résultats obtenus dans l'essai sont rassemblés dans les tableaux en annexe 2 (résultats à 24 heures) et en annexe 3 (résultats à 48 heures). La partie supérieure montre les données brutes obtenues ; les concentrations utilisées pour les calculs (concentrations calculées) sont indiquées en dessous. Après linéarisation au moyen de la méthode des Probits, on obtient les résultats suivants :

**$CE_{50}$-24h = 0,26 mg/l,**
avec un intervalle de confiance à 95 % égal à : 0,079 - 0,51 mg/l ($r^2$ = 0,806)

**$CE_{50}$-48h = 0,15 mg/l,**
avec un intervalle de confiance à 95 % indéterminé ($r^2$ = 0,868)

Elf Atochem S. A.
Centre d'Application de Levallois

## TECHNICAL SUMMARY

The acute toxicity (inhibition of mobility) of BENZYLMERCAPTAN for *Daphnia magna* was assessed according to the method C2 of the European Directive 92/69/CEE. The study was carried out in compliance with the Principles of OECD Good Laboratory Practices.

Daphnia were exposed in a static test to a concentration range of 0,08 to 8,45 mg/l, forming a geometric progression with a factor of 1,8. The test was performed with 5 daphnia per vessel. Since BENZYLMERCAPTAN is volatile, the test was performed using closed flasks as test glassware. In order to avoid volatilisation of BENZYLMERCAPTAN flasks were entirely filled with test solutions and closed with butyl rubber caps covered with PTFE.

For each exposure concentration, the percentage of immobilisation at 24 hours and 48 hours was recorded. The test concentrations of BENZYLMERCAPTAN were measured by CPG according to the analytical method described in the attached report. $EC_{50}$-24h and $EC_{50}$-48h were calculated with measured initial concentrations by regression analysis using the Probit/log model.

**The $EC_{50}$-24h was calculated to be 0,26 mg/l with 95 % confident interval ranging from 0,079 to 0,51 mg/l.**

**The $EC_{50}$-48h was calculated to be 0,15 mg/l with 95 % confident interval ranging indetermined.**

**The method was applied with respect to its quality criteria :**

- Immobilisation in the control did not exceed 10 % at the end of the test ;
- Concentration of dissolved oxygen in the test vessels remained above 2 mg/l at the end of the test and pH did not varied by more than 1 unit ;
- The concentrations of the test substance have been maintained to within 80 % of the initial concentration throughout the duration of the test.

**Reliability** : (1) valid without restriction
**Flag** : Critical study for SIDS endpoint
06.01.2004 (4)

**Type** : other: ECOSAR Predicted LC50
**Species** : other: Daphnid
**Exposure period** : 48 hour(s)
**Unit** : mg/l
**Analytical monitoring** :
**LC50** : c = 0.045
**Method** : other: calculated using EPIWIN v 3.10

| | | |
|---|---|---|
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | ECOSAR Program (v 0.99g).<br><br>The following physical parameters were used:<br>Molecular Weight: 124.2<br>Log Kow: 2.48 (KowWin estimate)<br>Water Solubility: 178.9 mg/L (calculated) |
| **Result** | : | ECOSAR Class: Thiols (mercaptans)<br>Organism: Daphnid<br>Duration: 48-hr<br>LC50: 0.045 mg/L (ppm) |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Benzenemethanethiol (CAS Number 100-53-8) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (14)

### 5.1.1 ACUTE ORAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 20 |
| **Vehicle** | : | |
| **Value** | : | = 493 mg/kg bw |
| **Method** | : | other |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : Comparable to OECD 401 "Acute Oral Toxicity."

**Result** :

TIME OF DEATH
Cumulative mortality Following Administration by dose:
132 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 0/5; Day 15 = 0/5

264 mg/kg: Day 1 = 0/5;Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 0/5; Day 15 = 0/5

528 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 3/5; Day 10 = 3/5; Day 15 = 3/5

1056 mg/kg: Day 1 = 3/5; Day 2 = 5/5

2112 mg/kg: Day 1 = 5/5 (all dead 6-10 hrs)

CLINICAL SIGNS: From paragraph comparing several thiols tested by injection, stated to be similar results for oral:
- Compounds had property of being soporific, the degree ranging from mild stupor to heavy sedation.
- These conditions were slight for the aromatic thiols. - The response of the thiol-injected rats was fairly uniform in that the symptomology of acute poisoning developed in the order of: restlessness, increased respiration, incoordination, muscular weakness, skeletal muscle paralysis in most cases (starting with hind limbs), heavy to mild cyanosis, lethargy and/or sedation, respiratory depression followed by coma and death in cases of lethal doses.

LD50 1 day = 985 mg/kg (confidence limits 702-1383 mg/kg)
LD50 15 day = 493 mg/kg (confidence limits 351-692 mg/kg)

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** :

DOSES
132 mg/kg
264 mg/kg
528 mg/kg
1056 mg/kg

ORAL ADMINISTRATION
- Doses per Time Period: Single oral dose - undiluted.
- Each of the thiols was administered by gavage to at least four groups of

five rats each.
- Rats were dosed at levels in geometric progression (factor 1.26 or 2.0) by introducing measured amounts of the test material from a hypodermic syringe and blunted needle (8 cm, 18 gauge) which was passed through the esophagus into the stomach.

EXPERIMENTAL ANIMALS
- Rats were used of the same stock and weight.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS
LD50 values were calculated by the method of Weil (1952).

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Test substance** : alpha Toluenethiol (benzyl mercaptan) - Eastman Grade, 97% pure.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
31.12.2003 (8) (16)

### 5.1.2 ACUTE INHALATION TOXICITY

| | | |
|---|---|---|
| **Type** | : | LC50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 36 |
| **Vehicle** | : | |
| **Exposure time** | : | 4 hour(s) |
| **Method** | : | other |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | Comparable to OECD 403 " Acute Inhalation Toxicity". |

**Result** : TIME OF DEATH
Cumulative Mortality During and After Exposure

58 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 0/6; 15 day = 0/6

98 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 0/6; 15 day = 0/6

130 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 0/6; 15 day = 0/6

145 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 0/6; 15 day = 0/6

185 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 0/6; 15 day = 1/6*
* One died day 13 with pneumonia.

235 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 0/6; 15 day = 1/6**
** One died day 7.

CLINICAL SIGNS : From paragraph comparing several thiols tested by inhalation:
- Maximal sublethal and lethal concentrations induced characteristic symptoms of toxicity, i.e. increased respiration and restlessness, incoordinated movement and staggering gait, muscular weakness, partial skeletal muscle paralysis beginning in the hind limbs, light to severe cyanosis, tolerance of prone position, and mild to heavy sedation.
- Fatal Responses usually followed one of two patterns:
(1) animals exposed to maximal lethal concentrations died from respiratory arrest while in or shortly after removal from the chamber, and
(2) those animals exposed to minimal lethal concentrations died while in a semiconscious condition of long duration. - The aromatic thiols induced some lethargy and sedation which was quickly terminated upon exposure to normal atmosphere.
- Most of the thiols were irritating to the mucus membranes within approximately 15 minutes after exposure to high concentrations as evidenced by their rubbing of the eyes and nose, eye closure, occasional sneezing, watering of the eyes, and retracting of the head.

LC50 Not Calculable -- Higher concentrations not used because of heavy condensation and other technical difficulties.

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** : alpha Toluenethiol (benzyl mercaptan) - Eastman Grade, 97% pure.

**Test substance** : DOSES
58 ppm
98 ppm
130 ppm
145 ppm
185 ppm
235 ppm

DOSE ADMINISTRATION
- Four hour exposure periods.
- The generation of thiol vapors was accomplished by either of two methods: (1) bubbling a stream of nitrogen gas (to prevent possible oxidation to sulfide) through a midget fritted-glass bubbler, which contained the liquid thiol, or (2) by passage of nitrogen into a borosilicate glass nebulizer which contained the thiol.
- Desired exposure concentrations of thiols were maintained in a glass chamber of approximately 18-liter capacity by varying the ratio of volume flow (liters/minute) of compressed air and compressed nitrogen.
- Prior to entering the chamber, the compressed air was scrubbed by passage through a fritted bubbler containing potassium dichromate in concentrated sulfuric acid, thence through a column of glass wool which was followed by a column of Drierite.
- From this it went into a mixing tube which received the thiol vapors by another inlet; the mixture then passed into the exposure chamber.

SAMPLING AND ANALYSIS OF EXPOSURE ATMOSPHERE
- During exposure periods the concentrations of thiols within the chamber were determined routinely by absorption of vapors in either iso-propyl alcohol or acetone containing an excess of silver nitrate and titrating the uncombined silver amperometrically according to the methods of Grimes, et al. (1955).
- Samples for analysis were collected in an Erlenmeyer flask containing an excess of silver nitrate of known normality (approximately 0.01 N) in 50 ml

of acetone or isopropyl alcohol; the choice of solvent was determined by the thiol used and its solubility therein.
- After the thiol vapors had been metered through this solution, the resulting precipitate (silver mercaptide) and other contents were quantitatively washed from the flask and the excess silver titrated amperometrically with standard dodecyl mercaptan (approximately 0.044 N).
- Accuracy of the sampling technique and analytical procedure as applied to this work was tested by vaporizing known amounts of thiols and was found to be within 2% of that calculated.

EXPERIMENTAL ANIMALS
- Six rats per dose group, averaging 200 +/- grams.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS: LC50 values by inhalation were calculated by the method of Miller and Tainter (1944) using logarithmic-probit graph paper.

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
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**Type** : LC50
**Species** : mouse
**Strain** : Swiss
**Sex** : male
**Number of animals** : 60
**Vehicle** :
**Exposure time** : 4 hour(s)
**Value** : 178 ppm
**Method** : other
**Year** : 1957
**GLP** : no
**Test substance** : other TS

**Method** : Comparable to OECD 403 " Acute Inhalation Toxicity".

**Result** : TIME OF DEATH
Cumulative Mortality During and After Exposure
58 ppm: 0-4 hr = 0/10; 24 hr = 0/10; 48 hr = 0/10; 15 day = 0/10

98 ppm: 0-4 hr = 0/10; 24 hr = 0/10; 48 hr = 0/10; 15 day = 0/10

130 ppm: 1-4 hr = 0/10; 24 hr = 0/10; 48 hr = 0/10; 15 day = 0/10

145 ppm: 0-4 hr = 0/10; 24 hr = 0/10; 48 hr = 0/10; 15 day = 0/10

185 ppm: 1-4 hr = 3/10; 24 hr = 3/10; 48 hr = 3/10; 15 day = 6/10*
* One died day 3, two died day 4.

235 ppm: 0-4 hr = 1/10; 24 hr = 10/10

CLINICAL SIGNS : From paragraph comparing several thiols tested by inhalation:
- Maximal sublethal and lethal concentrations induced characteristic symptoms of toxicity, i.e. increased respiration and restlessness (hyperactivity in mice), incoordinated movement and staggering gait, muscular weakness, partial skeletal muscle paralysis beginning in the hind limbs, light to severe cyanosis, tolerance of prone position, and mild to heavy sedation.
- Fatal Responses usually followed one of two patterns:
(1) animals exposed to maximal lethal concentrations died from respiratory arrest while in or shortly after removal from the chamber, and
(2) those animals exposed to minimal lethal concentrations died while in a semiconscious condition of long duration. - The aromatic thiols induced some lethargy and sedation which was quickly terminated upon exposure to normal atmosphere.
- Most of the thiols were irritating to the mucus membranes within approximately 15 minutes after exposure to high concentrations as evidenced by their rubbing of the eyes and nose, eye closure, occasional sneezing, watering of the eyes, and retracting of the head.

LC50 24 hr: 195 ppm (est)
LC50 15 day: 178 ppm (est)

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** : alpha Toluenethiol (benzyl mercaptan) - Eastman Grade, 97% pure.

**Test substance** : DOSES
58 ppm
98 ppm
130 ppm
145 ppm
185 ppm
235 ppm

DOSE ADMINISTRATION
- Four hour exposure periods.
- The generation of thiol vapors was accomplished by either of two methods: (1) bubbling a stream of nitrogen gas (to prevent possible oxidation to sulfide) through a midget fritted-glass bubbler, which contained the liquid thiol, or (2) by passage of nitrogen into a borosilicate glass nebulizer which contained the thiol.
- Desired exposure concentrations of thiols were maintained in a glass chamber of approximately 18-liter capacity by varying the ratio of volume flow (liters/minute) of compressed air and compressed nitrogen.
- Prior to entering the chamber, the compressed air was scrubbed by passage through a fritted bubbler containing potassium dichromate in concentrated sulfuric acid, thence through a column of glass wool which was followed by a column of Drierite.
- From this it went into a mixing tube which received the thiol vapors by another inlet; the mixture then passed into the exposure chamber.

SAMPLING AND ANALYSIS OF EXPOSURE ATMOSPHERE
- During exposure periods the concentrations of thiols within the chamber were determined routinely by absorption of vapors in either iso-propyl alcohol or acetone containing an excess of silver nitrate and titrating the uncombined silver amperometrically according to the methods of Grimes, et al. (1955).
- Samples for analysis were collected in an Erlenmeyer flask containing an excess of silver nitrate of known normality (approximately 0.01 N) in 50 ml

of acetone or isopropyl alcohol; the choice of solvent was determined by the thiol used and its solubility therein.
- After the thiol vapors had been metered through this solution, the resulting precipitate (silver mercaptide) and other contents were quantitatively washed from the flask and the excess silver titrated amperometrically with standard dodecyl mercaptan (approximately 0.044 N).
- Accuracy of the sampling technique and analytical procedure as applied to this work was tested by vaporizing known amounts of thiols and was found to be within 2% of that calculated.

EXPERIMENTAL ANIMALS
- Ten mice per dose group, averaging 25 to 28 grams.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS: LC50 values by inhalation were calculated by the method of Miller and Tainter (1944) using logarithmic-probit graph paper.

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
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### 5.1.3 ACUTE DERMAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD0 |
| **Species** | : | rat |
| **Strain** | : | Sprague-Dawley |
| **Sex** | : | male/female |
| **Number of animals** | : | 10 |
| **Vehicle** | : | |
| **Value** | : | >= 2000 mg/kg bw |
| **Method** | : | OECD Guide-line 402 "Acute dermal Toxicity" |
| **Year** | : | 1995 |
| **GLP** | : | yes |
| **Test substance** | : | other TS |

**Result** : MORTALITY: No death occurred at 2000 mg/kg.

CLINICAL SIGNS
- No clinical signs and no cutaneous reactions were observed during the study.
- General behavior and body weight was not affected.

PATHOLOGY: Macroscopic examination of the main organs of the animals revealed no apparent abnormalities.

Dermal LD0 of the test substance was higher than or equal to 2000 mg/kg in rats. (author)

**Source** : Elf Atochem Rotterdam B.V., Acute Dermal Toxicity in Rats - Benzyl

Mercaptan. Study performed by Centre International de Toxicologie (C.I.T.), Miserey, France.

**Test condition** : The test substance was applied in its original form to the dorsal area skin (10% surface area) of one group of ten Sprague-Dawley rats (five males and five females) at a dose of 2000 mg/kg. The test site was then covered by semi-occlusive dressing for 24 hours.

Clinical signs, mortality and body weight gain were checked for a period of 14 days following the single administration of the test substance.

All animals were subjected to necropsy.

TEST ANIMALS
- Rat, Sprague-Dawley ICO: OFA-SD (IOPS Caw).
- Age/weight: on the day of treatment, the animals were approximately eight weeks old, and had a mean body weight +/- standard deviation of 272 +/- 5 g for the males and 228 +/- 17 g for the females.
- Acclimatization: at least five days before the beginning of the study.

ENVIRONMENTAL CONDITIONS
- Temperature: 21 +/- 2 deg C
- Relative humidity: 30 to 70 percent
- Light/dark cycle: 12 h/12 h
- Ventilation: about 12 cycles/h of filtered, non-recycled air.
- The animals were housed in polycarbonate cages.
- The animals were housed individually during the treatment.

CLINICAL EXAMINATIONS
- The animals were observed frequently during the hours following administration of the test substance, for detection of possible treatment-related clinical signs.
- Thereafter, observation of the animals was made at least once a day.
- Type, time of onset and duration of clinical signs and local cutaneous reactions were recorded for each animal individually.
- Body weight: animals were weighed individually just before administration of the test substance on day 1 and then on days 8 and 15.

NECROPSY
- On day 15, all animals were killed by CO2 inhalation in excess and a macroscopic examination was performed.
- After opening the thoracic and abdominal cavities, a macroscopic examination of the main organs (digestive tract, heart, kidneys, liver, lungs, pancreas, spleen, and any other organs with obvious abnormalities) was performed.
- In case of macroscopic lesions, organ samples were taken and preserved in 10% buffered formalin.
- No microscopic examination was performed.

**Test substance** : Benzyl mercaptan (CAS Number 100-53-8) supplied by Elf Atochem S.A. 99.3% pure (sample contained 0.04% Dibenzylsulphide and 0.13% Dibenzyldisulphide).

**Reliability** : (1) valid without restriction
**Flag** : Critical study for SIDS endpoint
31.12.2003 (5)

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 20 |
| **Vehicle** | : | |
| **Route of admin.** | : | i.p. |
| **Exposure time** | : | unspecified |
| **Value** | : | = 373 mg/kg bw |
| **Method** | : | Intraperitoneal LD50 |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Result** :

TIME OF DEATH
Cumulative Mortality Following Administration
132 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 0/5; Day 15 = 0/5

264 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 1/5; Day 15 = 1/5

529 mg/kg: Day 1 = 4/5; Day 2 = 4/5; Day 3 = 4/5; Day 5 = 4/5; Day 10 = 4/5; Day 15 = 4/5

1058 mg/kg: Day 1 = 5/5 (All dead at 7 hrs.)

CLINICAL SIGNS : From paragraph comparing several thiols tested by injection:
- Compounds had property of being soporific, the degree ranging from mild stupor to heavy sedation. These conditions were slight for the aromatic thiols.
- The response of the thiol-injected rats was fairly uniform in that the symptomology of acute poisoning developed in the order of: restlessness, increased respiration, incoordination, muscular weakness, skeletal muscle paralysis in most cases (starting with hind limbs), heavy to mild cyanosis, lethargy and/or sedation, respiratory depression followed by coma and death in cases of lethal doses.

The LD50 1 Day (ip) = 429 mg/kg (confidence limits 325 - 566 mg/kg).
The LD50 15 Day (ip) = 373 mg/kg (confidence limit 252 - 553 mg/kg).

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** :

DOSES
132 mg/kg
264 mg/kg
529 mg/kg
1058 mg/kg

Dose ADMINISTRATION
- Doses per Time Period: Single intraperitoneal - undiluted.
- Groups of at least five Wistar-derived rats, each weighing on the average 200 +/- 20 grams were injected intraperitoneally at dosage levels differing by a factor of either 1.26 or 2.0 in a geometric series, according to Weil (1952).

EXPERIMENTAL ANIMALS
- Rats were used of the same stock and weight.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS
LD50 values were calculated by the method of Weil (1952).

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Test substance** : alpha Toluenethiol (benzyl mercaptan) - Eastman Grade, 97% pure.

**Reliability** : (2) valid with restrictions
31.12.2003 (8) (16)

### 5.2.1 SKIN IRRITATION

| | | |
|---|---|---|
| **Species** | : | rabbit |
| **Concentration** | : | undiluted |
| **Exposure** | : | Semiocclusive |
| **Exposure time** | : | 4 hour(s) |
| **Number of animals** | : | 3 |
| **PDII** | : | |
| **Result** | : | not irritating |
| **EC classification** | : | not irritating |
| **Method** | : | OECD Guide-line 404 "Acute Dermal Irritation/Corrosion" |
| **Year** | : | 1996 |
| **GLP** | : | yes |
| **Test substance** | : | other TS |

**Result** : Mean scores over 24, 48, and 72 hours for individual animal were 2.0, 1.7, and 1.0 for erythema and 1.3, 0.0, and 0.0 for edema.

- In one animal, very slight erythema was observed from day 2 up to day 5.
- In another rabbit, slight erythema was noted from day 2 up to day 5. It was accompanied with a slight oedema on days 2 and 3.
- In the third rabbit, very slight to slight erythema was observed up to day 8.
- Dryness of the skin was noted in all animals from day 3 or 4 up to day 8 (two animals) or until the end of the study (day 15, one animal).

**Source** : Elf Atochem Rotterdam B.V., Acute Dermal Irritation in Rabbits - Benzyl Mercaptan. Study performed by Centre International de Toxicologie (C.I.T.), Miserey, France.

**Test condition** : CONCENTRATION: The test substance was administered in its original form (undiluted).

TEST ANIMALS
- Male New Zealand White rabbits.
- Weight: on the day of treatment, the animals had a mean body weight +/- standard deviation of 2.6 +/- 0.2 kg.
- Acclimatization: at least five days before the beginning of the study.

ENVIRONMENTAL CONDITIONS
- Temperature: 18 +/- 3 deg C
- Relative humidity: 30 to 70 percent
- Light/dark cycle: 12 h/12 h
- Ventilation: about 12 cycles/h of filtered, non-recycled air.
- The animals were housed in polystyrene cages.
- The animals were housed individually during the treatment.

TREATMENT
- The day before treatment, the flanks of each animal were clipped using electric clippers.
- The skin was examined in order to use only animals without any signs of cutaneous irritation.
- A single dose of 0.5 ml of the test substance was applied to a 6 cm2 dry gauze pad which was then applied to the right flank of the animals for four hours.
- The test substance and the gauze pad were held in contact with the skin by means of an adhesive hypoallergenic aerated semi-occlusive dressing and a restraining bandage.
- No residual test substance was noted at removal of the dressing.

CONTROLS: The untreated skin served as control.

CUTANEOUS EXAMINATIONS
- The skin was examined approximately one hour, 24, 48, and 72 hours after removal of the dressing.
- Any change in the animals' behaviour was noted.

Scoring:
- Dermal irritation was evaluated for each animal according to the following scoring scale:

Erythema and eschar formation:
- No erythema --> 0
- Very slight erythema (barely perceptible) --> 1
- Well-defined erythema --> 2
- Moderate to severe erythema --> 3
- Severe erythema (beet redness) to slight eschar formation (injuries in depth) --> 4

Edema formation
- No edema --> 0
- Very slight edema (barely perceptible) --> 1
- Slight edema (edges of area well-defined by definite raising) --> 2
- Moderate edema (raised approximately 1 mm) --> 3
- Severe edema (raised more than 1 mm and extending beyond area of exposure) --> 4

**Test substance** : Benzyl mercaptan (CAS Number 100-53-8) supplied by Elf Atochem S.A. 99.3% pure (sample contained 0.04% Dibenzylsulphide and 0.13% Dibenzyldisulphide).

**Reliability** : (1) valid without restriction
31.12.2003 (6)

## 5.3 SENSITIZATION

**Type** : Guinea pig maximization test
**Species** : guinea pig

| | | |
|---|---|---|
| **Concentration** | : | Induction 10 % active substance intracutaneous<br>Induction undiluted occlusive epicutaneous<br>Challenge undiluted occlusive epicutaneous |
| **Number of animals** | : | 30 |
| **Vehicle** | : | other: paraffin oil |
| **Result** | : | not sensitizing |
| **Classification** | : | not sensitizing |
| **Method** | : | OECD Guide-line 406 "Skin Sensitization" |
| **Year** | : | 1996 |
| **GLP** | : | yes |
| **Test substance** | : | other TS |

**Result** :

Conclusion: Under experimental conditions and according to the maximization method of Magnusson and Kligman (1969), no cutaneous reactions attributable to the sensitization potential of Benzyl Mercaptan were observed in guinea pigs.

- No clinical signs and no treatment-related deaths were noted during the study.
- After the challenge application, comparable slight to severe skin reactions were observed in the treated and control groups. Based on clinical observation, differentiation between an irritant effect of the test substance and a sensitization effect could not be made since the skin reactions were present in the control group at approximately the same level of severity.
- Due to the severity of the skin damage observed, a second challenge application was considered unethical.
- The animals were killed and microscopic examination of skin samples was performed: the morphological characteristics and the severity of the microscopic findings found in the skin of the treated or control animals were comparatively similar. The major findings were degeneration/necrosis of epidermis and inflammatory cell infiltration, mainly of granulocytes, together with exocytosis and exudation somtimes in lacunae.
- The above-mentioned findings are those expected in cases of skin irritation.

Positive Control: The guinea-pigs which were used in a recent study, showed a satisfactory sensitization response in 100% of the animals using a positive sensitizer (2,4-dinitro chlorobenzene).

RESULTS FOR INDIVIDUAL ANIMALS:
Results presented as: Erythema LF / Erythema RF / Edema LF / Edema RF
(Abbreviations: LF = left flank (control); RF = right flank (treated); A = crusts; S = dryness of the skin; DT = tissular destruction; P = pallor of the skin; "-" = dead animal.)

Treated Group 2 - Males #06 through #15,
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 0,P / 0 / 4 48 hrs: 0 / 1,P / 0 / 2 72 hrs: 0 / 1,P / 0 / 2
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 0,P / 0 / 4 48 hrs: 0 / 1,P / 0 / 2 72 hrs: 0 / 1,P / 0 / 2
24 hrs: 0 / 1 / 0 / 0 48 hrs: 0 / 1,S / 0 / 0 72 hrs: 0 / 1,S / 0 / 0
24 hrs: 0 / 0,A / 0 / 0 48 hrs: 0 / DT,A / 0 / 0 72 hrs: 0 / DT,A / 0 / 0
24 hrs: 0,S / 0,S / 0 / 0 48 hrs: 0,S / 0,S / 0 / 0 72 hrs: 0,S / 0,S / 0 / 0
24 hrs, 48 hrs, and 72 hrs: - / - / - / -
24 hrs: 0 / 0,S / 0 / 0 48 hrs: 0 / 0 / 0 / 0 / 72 hrs: 0 / 0 / 0 / 0

Treated Group 2 - Females #21 through #30,
24 hrs: 0 / 0,S,A / 0 / 0 48 hrs: 0 / 1,S,A / 0 / 2 72 hrs: 0 / 1,S / 0 / 0
24 hrs: 0 / 0,P / 0 / 0 48 hrs: 0 / 2,P / 0 / 4 72 hrs: 0 / 2,P / 0 / 4
24 hrs: 0,S / 0,S / 0 / 0 48 hrs: 0,S / 0,S / 0 / 0 72 hrs: 0 / 0,S / 0 / 0

24 hrs: 0 / 1 / 0 / 0 48 hrs: 0 / 0,S / 0 / 0 72 hrs: 0 / 0,S / 0 / 0
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0,S / 0 / 0 72 hrs: 0 / 0,S / 0 / 0
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / DT,A / 0 / 2 72 hrs: 0 / A / 0 / 2
24 hrs: 0 / 0,A / 0 / 0 48 hrs: 0 / 4,S,A / 0 / 2 72 hrs: 0 / 3,S,A / 0 / 2
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 1,S / 0 / 0 48 hrs: 0 / 4,A / 0 / 2 / 72 hrs: 0 / 3,A / 0 / 2
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0,S / 0 / 0 / 72 hrs: 0 / 0,S / 0 / 0

Control Group 1 - Males #01 through #05,
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 1 / 0 / 2 72 hrs: 0 / 2 / 0 / 0
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 1,S / 0 / 2 72 hrs: 0 / 1,S / 0 / 2
24 hrs: 0 / 0,P / 0 / 4 48 hrs: 0 / 4 / 0 / 2 72 hrs: 0 / 0,P / 0 / 4
24 hrs: 0 / 1 / 0 / 0 48 hrs: 0 / 1 / 0 / 0 72 hrs: 0 / 1 / 0 / 0

Control Group 1 - Females #16 through #20,
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 1,S / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0,S / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 0,P / 0 / 4 48 hrs: 0 / 0,P,A / 0 / 4 72 hrs: 0 / 0,P,A / 0 / 2
24 hrs: 0 / 0 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0
24 hrs: 0 / 1 / 0 / 0 48 hrs: 0 / 0 / 0 / 0 72 hrs: 0 / 0 / 0 / 0

**Source** : Elf Atochem Rotterdam B.V., Skin Sensitization Test in Guinea-Pigs (Maximization method of Magnusson, B. and Kligman, A.M.) - Benzyl Mercaptan. Study performed by Centre International de Toxicologie (C.I.T.), Miserey, France.

**Test condition** : TEST ANIMALS
- Species and Strain: Dunkin-Hartley guinea-pigs (15 males and 15 nulliparous and non-pregnant females).
- Age and Weight: on day 1, the animals were approximately three months old and had a mean body weight +/- standard deviation of 312 +/- 16 g for the males and 352 +/- 29 g for the females.
- Acclimatization: at least five days before the beginning of the study.

ENVIRONMENTAL CONDITIONS
- Temperature: 21 +/- 2 deg C
- Relative humidity: 30 to 70 percent
- Light/dark cycle: 12 h/12 h
- Ventilation: about 12 cycles/h of filtered, non-recycled air.
- The animals were housed in polycarbonate cages with dust-free sawdust provided as litter.
- The animals were housed individually during the treatment.

METHODS
-Thirty guinea-pigs were allocated to two groups: a control group 1 (five males and five females) and a treated group 2 (ten males and ten females).
- On day 1, in the dorsal region between the shoulders, intradermal injections of Freund's complete adjuvant mixed with the test substance (treated group) or the vehicle (control group) were prepared.
- On day 7, the same region received a topical application of sodium laurylsulfate in vaseline (10% w/w) in order to induce local irritation.
- On day 8, this same test site was treated by topical application of the test substance (treated group) or the vehicle (control group) and was covered by an occlusive dressing for 48 hours.
- After a rest period of 12 days, all animals of the treated and control groups were challenged by a topical application of the test substance to the right flank. The left flank served as control and received the vehicle only.
- Test substance and vehicle were maintained under an occlusive dressing for 24 hours.

Test Substance Concentrations:

- Induction (treated group)
--- Intradermal injections: Benzyl Mercaptan at 10% (w/w) in paraffin oil
--- Topical application: Benzyl Mercaptan undiluted.

- Challenge (all groups)
--- topical application: Benzyl Mercaptan undiluted.

CLINICAL AND MICROSCOPIC EXAMINATIONS
- Skin reactions were evaluated approximately 24, 48, and 72 hours later.
- At the end of the study, animals were killed and cutaneous samples were taken from the challenge application sites from all the animals. Histological examinations were performed on the samples of cutaneous tissue, on the right flank, from all the animals of the control and treated groups.

POSITIVE CONTROL
- The sensitivity of the guinea-pigs in C.I.T. experimental conditions were confirmed in a recent study with a positive sensitizer: 2,4-dinitro chlorobenzene. During induction period, the test substance was applied at 0.1% (day 1) and 1% (day 8) concentrations. At cutaneous challenge application, 1% (w/w) was tested on the right flank.

**Test substance** : Benzyl mercaptan (CAS Number 100-53-8) supplied by Elf Atochem S.A. 99.3% pure (sample contained 0.04% Dibenzylsulphide and 0.13% Dibenzyldisulphide).

**Reliability** : (1) valid without restriction
02.01.2004 (7) (11)

## 5.5 GENETIC TOXICITY 'IN VITRO'

| | | |
|---|---|---|
| **Type** | : | Bacterial reverse mutation assay |
| **System of testing** | : | Bacterial, Strains: TA1535, TA100, TA1537, TA1538, TA98. |
| **Concentration** | : | Not given |
| **Cycotoxic conc.** | : | |
| **Metabolic activation** | : | with and without |
| **Result** | : | negative |
| **Method** | : | other |
| **Year** | : | 1982 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : Comparable to OECD 471 "Genetic Toxicology: Salmonella typhimurium, Reverse Mutation Assay."

**Result** : Negative

Statistical Results not given.

**Source** : Study of Artificial Flavouring Substances for Mutagenicity in the Salmonella/Microsome, BASC and Micronucleus Tests (Wild et al., 1983).

**Test condition** : Methods are general methods for several compounds studied

TEST DESIGN
- 5 doses in each strain, with and without activation.
- Standard plate procedure followed (Ames et al., 1975)
- Vogel-Bonner medium used throughout (Vogel & Bonner, 1956)
- Plates incubated for 48 hours.

NUMBER OF REPLICATES: Tested at least twice

POSITIVE AND NEGATIVE CONTROLS:
- Positive Controls: sodium azide, benzo[a]pyrene.
- Positive controls were run in each experiment.
- Over a period of 2 yr, the numbers of revertants/plate in positive controls were in the following ranges: with sodium azide, at 0.5 ug/plate, 430-760 in TA1535, 400-700 in TA100; with benzo[a]pyrene, at 5 ug/plate, 865-1210 in TA100, 235-350 in TA1537, 410-590 in TA1538, 660-1000 in TA98.

SOLVENT: Dimethylsulphoxide was used as solvent for test chemicals that were poorly soluble in water.

METABOLIC ACTIVATION
- S-9 liver fractions were prepared from Aroclor pre-treated rats (Aroclor 1254, 500 mg/kg ip) and adjusted to 25 mg protein/ml; 0.5 ml S-9 mix, equivalent to 50 µl S-9.

STATISTICAL METHODS
- Statistical significance was determined according to the methods of Kastenbaum & Bowman (1970).
- With regards to the Ames tests, results that met the following additional criteria were regarded as positive (+): a reproducible, dose-related and at least two-fold elevation of the spontaneous revertant frequency. Agents producing reproducible, dose-related and significant (P</= 0.01) but less than two-fold elevations were classified as marginally mutagenic under the experimental conditions.

**Test substance** : Benzylmercaptan (toluene-alpha-thiol) supplied by ICN-K&K, Plainview, NY. Purity not given.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
31.12.2003 (1) (10) (15) (17)

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(4) Centre D'Application de Levallois. 1997. Benzyl Mercaptan, Toxicite Aiguë vis-à-vis des Daphnies. Study No. 4353/96/A (31-January-1997). (Elf Atochem S.A.)

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## 7.1 END POINT SUMMARY

## 7.2 HAZARD SUMMARY

## 7.3 RISK ASSESSMENT

# Appendix II

# Phenyl Mercaptan

# I U C L I D

# Data Set

| | | |
|---|---|---|
| **Existing Chemical** | : | ID: 108-98-5 |
| **CAS No.** | : | 108-98-5 |

**Producer Related Part**

| | | |
|---|---|---|
| **Company** | : | Chevron Phillips Chemical Company LP |
| **Creation date** | : | 24.11.2003 |

**Substance Related Part**

| | | |
|---|---|---|
| **Company** | : | Chevron Phillips Chemical Company LP |
| **Creation date** | : | 24.11.2003 |
| **Memo** | : | |
| **Printing date** | : | 02.01.2004 |
| **Revision date** | : | |
| **Date of last Update** | : | 02.01.2004 |
| **Number of Pages** | : | 4 |
| **Chapter (profile)** | : | Chapter: 1, 2, 3, 4, 5, 7 |
| **Reliability (profile)** | : | Reliability: without reliability, 1, 2, 3, 4 |
| **Flags (profile)** | : | Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS |

### 1.0.1 OECD AND COMPANY INFORMATION

| | | |
|---|---|---|
| **Type** | : | other |
| **Name** | : | Chevron Phillips Chemical Company LP |
| **Partner** | : | |
| **Date** | : | |
| **Street** | : | 10001 Six Pines Drive |
| **Town** | : | 77380 The Woodlands, TX |
| **Country** | : | United States |
| **Phone** | : | |
| **Telefax** | : | |
| **Telex** | : | |
| **Cedex** | : | |

24.11.2003

### 1.2 SYNONYMS

Benzenethiol
24.11.2003

Phenyl Mercaptan
24.11.2003

Thiophenol
24.11.2003

## 2.1 MELTING POINT

| | | |
|---|---|---|
| **Value** | : | = -14.9 ° C |
| **Sublimation** | : | |
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | CRC Handbook of Chemistry and Physics (Lide, D.R., 2001-2002, 82nd ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

24.11.2003 (15)

| | | |
|---|---|---|
| **Value** | : | = -14.9 ° C |
| **Sublimation** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Remarks** | | Selected Melting Point (calculated mean value) was -31.86 ºC. |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | MPBWIN (v 1.40) Program, Experimental Melting Point. |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5). |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (32)

| | | |
|---|---|---|
| **Value** | : | = -14.8 ° C |
| **Sublimation** | : | |
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | Patty's Toxicology (Bingham, E., 2001, 5th ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

24.11.2003 (4)

## 2.2 BOILING POINT

| | | |
|---|---|---|
| **Value** | : | = 168.7 ° C |
| **Decomposition** | : | |
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | Patty's Toxicology (Bingham, E., 2001, 5th ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

24.11.2003 (4)

| | | |
|---|---|---|
| **Value** | : | = 169.1 ° C at |
| **Decomposition** | : | |

| | | |
|---|---|---|
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | CRC Handbook of Chemistry and Physics (Lide, D.R., 2001-2002, 82nd ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

24.11.2003 (15)

| | | |
|---|---|---|
| **Value** | : | = 169.1 ° C |
| **Decomposition** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | MPBWIN (v 1.40) Program, Experimental Boiling Point. |
| **Remarks** | | The Boiling Point was calculated to be 176.14 ºC using the Adapted Stein & Brown Method. |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5). |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (32)

| | | |
|---|---|---|
| **Value** | : | = 169.5 ° C |
| **Decomposition** | : | |
| **Method** | : | other: no data |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | Sax's Dangerous Properties of Industrial Materials (Lewis, 2000, 10th ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5), purity not given |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

24.11.2003 (14)

## 2.4 VAPOUR PRESSURE

| | | |
|---|---|---|
| **Value** | : | = 2.66645 hPa at 25° C |
| **Decomposition** | : | |
| **Method** | | |
| **Year** | : | |
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Source** | : | Patty's Toxicology (Bingham, E., 2001, 5th ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (4)

| | | |
|---|---|---|
| **Value** | : | = 2.57 hPa at 25° C |
| **Decomposition** | : | |
| **Method** | | other (calculated): EPIWIN v 3.10 |
| **Remarks** | | The Selected Vapor Pressure was calculated to be 1.63 mmHg (2.17316 hPa) at 25 ºC using the mean of Antoine & Grain methods. |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : MPBWIN (v 1.40) Program, Experimental Vapor Pressure.
**Source** : EPI Suite v 3.10.
**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).
**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (32)

## 2.5 PARTITION COEFFICIENT

**Log pow** : = 2.52
**Method** other (calculated): no data
**Year** : 1989
**GLP** : no
**Test substance** : other TS
**Source** : Octanol-water partition coefficients of simple organic compounds (Sangster, 1989 in J Phys Chem Ref Data).
**Test substance** : Phenylmercaptan (Thiophenol) CAS Number 108-98-5, Purity not given.
**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
24.11.2003 (22)

**Log pow** : = 2.52
**Method** other (calculated): EPIWIN v 3.10
**Remarks** The estimated Log Kow was calculated to be 2.69.
**Year** : 2003
**GLP** : no
**Test substance** : other TS
**Method** : WSKOW v 1.40 - Experimental Log Kow.
**Source** : EPI Suite v 3.10.
**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5)
**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (32)

## 2.6.1 WATER SOLUBILITY

**Value** : = 835 mg/l at 25 ° C
**Qualitative** : moderately soluble (100-1000 mg/L)
**Pka** :
**PH** :
**Method** : other: EPIWIN v 3.10
**Remarks** The estimated Water Solubility was calculated to be 765.5 mg/L at 25 ºC.
**Year** : 2003
**GLP** : no
**Test substance** : other TS
**Method** : WSKOW v 1.40 - Experimental Water Solubility.
**Source** : EPI Suite v 3.10.
**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).
**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (32)

**Value** : = 1
**Qualitative** :
**Pka** :
**PH** :
**Method** : other: no data
**Year** :

| | | |
|---|---|---|
| **GLP** | : | no data |
| **Test substance** | : | other TS |
| **Result** | : | Solubility in H2O = 1;<br>Solubility in EtOh = 3 |
| **Source** | : | CRC Handbook of Chemistry and Physics (Lide, D.R., 2001-2002, 82nd ed.) |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5) |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

31.12.2003 (15)

| | | |
|---|---|---|
| **Value** | : | |
| **Qualitative** | : | |
| **Pka** | : | 6.62 at 25 ° C |
| **PH** | : | |
| **Source** | : | Ionisation Constants of Organic Acids in Aqueous Solution (Serjeant and Dempsey, 1979) |
| **Test substance** | : | Benzenethiol (Thiophenol), purity not noted |
| **Flag** | : | Critical study for SIDS endpoint |

24.11.2003 (29)

### 3.1.1 PHOTODEGRADATION

| | | |
|---|---|---|
| **Type** | : | other |
| **Light source** | : | |
| **Light spect.** | : | |
| **Rel. intensity** | : | |
| **Deg. Product** | : | |
| **Method** | : | other (calculated): EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | AOP Program (v 1.90). |
| **Result** | : | Overall OH Rate Constant = 11.32 E-12 cm3/molecule-sec<br>Half-Life = 0.945 Days (12-hr day; 1.5E6 OH/cm3)<br>Half-Life = 11.34 Hrs |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5). |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

05.12.2003 (32)

### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

| | | |
|---|---|---|
| **Type** | : | fugacity model level III |
| **Media** | : | other: air-water-soil-sediment |
| **Air (level I)** | : | |
| **Water (level I)** | : | |
| **Soil (level I)** | : | |
| **Biota (level II / III)** | : | |
| **Soil (level II / III)** | : | |
| **Method** | : | other: EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **Method** | : | Used EPIWIN v 3.10. The following physical properties were used as the model input parameters:<br>Molecular Wt: 110.17<br>Henry's LC: 0.000335 atm-m3/mole (Henry experimental database)<br>Vapor Pressure: 1.63 mm Hg (Mpbpwin program)<br>Log KOW: 2.52 (Kowwin program)<br>Soil Koc: 136 (calc by model) |
| **Result** | : | Results are provided in the following format:<br>Compartment / 100% to Air / 100% to Water / 100% to Soil / Equally to Each Compartment<br><br>Air / 94.4% / 3.43% / 1.01% / 5.37%<br>Water / 4.58% / 96.0% / 1.61% / 34.2%<br>Soil / 0.993% / 0.0361% / 97.4% / 60.3%<br>Sediment / 0.025% / 0.523% / 0.0088% / 0.186%<br><br>Air: half life = 22.92 hr; emissions = 1000 kg/hr |

Water: half life = 360 hr; emissions = 1000 kg/hr
Soil: half life = 360 hr; emissions = 1000 kg/hr
Sediment: half life = 1.44E+3 hr; emissions = 0 kg/hr

Persistence when distributed equally to each compartment = 231 hr (Emissions (kg/hr) = 1000 to air, 1000 to water, 1000 to soil, and 0 to sediment)

**Source** : EPI Suite v 3.10.

**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (32)

## 3.7 BIOACCUMULATION

**BCF** : = 17.39
**Elimination** :
**Method** : other: EPIWIN v 3.10
**Year** : 2003
**GLP** : no
**Test substance** : other TS

**Method** : BCF Program (v 2.14).

**Remark** : Estimated Log BCF = 1.240

Estimated Koc = 268 (using PCKOC Program (v 1.66)

**Source** : EPI Suite v 3.10.

**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).

**Reliability** : (2) valid with restrictions
05.12.2003 (32)

## 4.1 ACUTE/PROLONGED TOXICITY TO FISH

| | | |
|---|---|---|
| **Type** | : | other: ECOSAR Predicted LC50 |
| **Species** | : | other: Fish |
| **Exposure period** | : | 14 day |
| **Unit** | : | mg/l |
| **Analytical monitoring** | : | |
| **LC50** | : | c = 37.076 |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : ECOSAR Program (v 0.99g).

The following physical parameters were used:
Molecular Weight: 110.17
Log Kow: 2.69 (KowWin estimate)
Water Solubility: 96.89 mg/L (calculated)

**Result** : ECOSAR Class: Neutral Organic SAR (Baseline Toxicity)
Organism: Fish
Duration: 14-day
LC50: 37.076 mg/L (ppm)

**Source** : EPI Suite v 3.10.

**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (32)

| | | |
|---|---|---|
| **Type** | : | other: ECOSAR Predicted LC50 |
| **Species** | : | other: Fish |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **Analytical monitoring** | : | |
| **LC50** | : | c = 6.082 |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : ECOSAR Program (v 0.99g).

The following physical parameters were used:
Molecular Weight: 110.17
Log Kow: 2.69 (KowWin estimate)
Water Solubility: 96.89 mg/L (calculated)

**Result** : ECOSAR Class: Phenols
Organism: Fish
Duration: 96-hr
LC50: 6.082 mg/L (ppm)

**Source** : EPI Suite v 3.10.

**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).

| | | |
|---|---|---|
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

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## 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

| | | |
|---|---|---|
| **Type** | : | other: ECOSAR Predicted LC50 |
| **Species** | : | other: Daphnid |
| **Exposure period** | : | 48 hour(s) |
| **Unit** | : | |
| **Analytical monitoring** | : | |
| **LC50** | : | c = 3.097 |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | ECOSAR Program (v 0.99g).<br><br>The following physical parameters were used:<br>Molecular Weight: 110.17<br>Log Kow: 2.69 (KowWin estimate)<br>Water Solubility: 96.89 mg/L (calculated) |
| **Result** | : | ECOSAR Class: Phenols<br>Organism: Daphnid<br>Duration: 48-hr<br>LC50: 3.097 mg/L (ppm) |
| **Source** | : | EPI Suite v 3.10. |
| **Test substance** | : | Phenyl Mercaptan (CAS Number 108-98-5). |
| **Reliability** | : | (2) valid with restrictions |
| **Flag** | : | Critical study for SIDS endpoint |

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## 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

| | | |
|---|---|---|
| **Species** | : | other algae |
| **Endpoint** | : | other: ECOSAR Predicted EC50 |
| **Exposure period** | : | 96 hour(s) |
| **Unit** | : | mg/l |
| **Analytical monitoring** | : | |
| **EC50** | : | c = 13.41 |
| **Method** | : | other: calculated using EPIWIN v 3.10 |
| **Year** | : | 2003 |
| **GLP** | : | no |
| **Test substance** | : | other TS |
| **Method** | : | ECOSAR Program (v 0.99g).<br><br>The following physical parameters were used:<br>Molecular Weight: 110.17<br>Log Kow: 2.69 (KowWin estimate)<br>Water Solubility: 96.89 mg/L (calculated) |
| **Result** | : | ECOSAR Class: Phenols |

Organism: Green Algae
Duration: 96-hr
EC50: 13.410 mg/L (ppm)

**Source** : EPI Suite v 3.10.

**Test substance** : Phenyl Mercaptan (CAS Number 108-98-5).

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
05.12.2003 (32)

### 5.1.1 ACUTE ORAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 20 |
| **Vehicle** | : | other: Ethanol as 8% v/v solution |
| **Value** | : | = 46.2 mg/kg bw |
| **Method** | : | other |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : Comparable to OECD 401 "Acute Oral Toxicity."

**Result** :

TIME OF DEATH
Cumulative mortality Following Administration by dose:
21.6 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 0/5; Day 15 = 0/5

43 mg/kg: Day 1 = 3/5; Day 2 = 3/5; Day 3 = 3/5; Day 5 = 3/5; Day 10 = 3/5; Day 15 = 3/5

86.2 mg/kg: Day 1 = 4/5; Day 2 = 4/5; Day 3 = 4/5; Day 5 = 4/5; Day 10 = 4/5; Day 15 = 4/5

172.5 mg/kg: Day 1 = 5/5 (All dead at 5 hrs).

CLINICAL SIGNS: From paragraph comparing several thiols tested by injection, stated to be similar results for oral:
- Compounds had property of being soporific, the degree ranging from mild stupor to heavy sedation.
- These conditions were slight for the aromatic thiols. - The response of the thiol-injected rats was fairly uniform in that the symptomology of acute poisoning developed in the order of: restlessness, increased respiration, incoordination, muscular weakness, skeletal muscle paralysis in most cases (starting with hind limbs), heavy to mild cyanosis, lethargy and/or sedation, respiratory depression followed by coma and death in cases of lethal doses.

LD50 = 46.2 mg/kg (confidence limits 29.8 - 71.6 mg/kg)

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** :

DOSES
21.6 mg/kg
43.0 mg/kg
86.2 mg/kg
172.5 mg/kg

ORAL ADMINISTRATION
- Doses per Time Period: Single oral dose in Ethanol as 8% v/v solution.
- Each of the thiols was administered by gavage to at least four groups of five rats each.
- Rats were dosed at levels in geometric progression (factor 1.26 or 2.0) by introducing measured amounts of the test material from a hypodermic

syringe and blunted needle (8 cm, 18 gauge) which was passed through the esophagus into the stomach.

EXPERIMENTAL ANIMALS
- Rats were used of the same stock and weight.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS
LD50 values were calculated by the method of Weil (1952).

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Test substance** : Benzenethiol (phenyl mercaptan), highest purity Eastman Grade.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
31.12.2003 (10) (33)

### 5.1.2 ACUTE INHALATION TOXICITY

| | | |
|---|---|---|
| **Type** | : | LC50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 46 |
| **Vehicle** | : | |
| **Exposure time** | : | 4 hour(s) |
| **Value** | : | = 33 ppm |
| **Method** | : | other |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : Comparable to OECD 403 " Acute Inhalation Toxicity".

**Result** : TIME OF DEATH
Cumulative Mortality During and After Exposure

20 ppm: 0-4 hr = 0/5; 24 hr = 0/5; 48 hr = 0/5; 15 day = 0/5

31 ppm: 0-4 hr = 0/10; 24 hr = 0/10; 48 hr = 0/10; 15 day = 5/10

41 ppm: 0-4 hr = 0/6; 24 hr = 0/6; 48 hr = 1/6; 15 day = 4/6

52 ppm: 0-4 hr = 0/5; 24 hr = 0/5; 48 hr = 2/5; 15 day = 5/5

79 ppm: 0-4 hr = 0/10; 24 hr = 1/10; 48 hr = 3/10; 15 day = 10/10*
* 7 deaths between days 3 and 8 - some pneumonia.

132 ppm: 0-4 hr = 10/10 (all dead in 3 hrs).

CLINICAL SIGNS : From paragraph comparing several thiols tested by

inhalation:
- Maximal sublethal and lethal concentrations induced characteristic symptoms of toxicity, i.e. increased respiration and restlessness, incoordinated movement and staggering gait, muscular weakness, partial skeletal muscle paralysis beginning in the hind limbs, light to severe cyanosis, tolerance of prone position, and mild to heavy sedation.
- Fatal Responses usually followed one of two patterns:
(1) animals exposed to maximal lethal concentrations died from respiratory arrest while in or shortly after removal from the chamber, and
(2) those animals exposed to minimal lethal concentrations died while in a semiconscious condition of long duration. - The aromatic thiols induced some lethargy and sedation which was quickly terminated upon exposure to normal atmosphere.
- Most of the thiols were irritating to the mucus membranes within approximately 15 minutes after exposure to high concentrations as evidenced by their rubbing of the eyes and nose, eye closure, occasional sneezing, watering of the eyes, and retracting of the head.

LC50 48 hour = 59 ppm (Confidence Limits 50.7 - 67.3 ppm)
LC50 15 day = 33 ppm (Confidence Limits 29.6 - 36.4 ppm)

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test substance** : DOSES
20 ppm
31 ppm
41 ppm
52 ppm
79 ppm
132 ppm

DOSE ADMINISTRATION
- Four hour exposure periods.
- The generation of thiol vapors was accomplished by either of two methods: (1) bubbling a stream of nitrogen gas (to prevent possible oxidation to sulfide) through a midget fritted-glass bubbler, which contained the liquid thiol, or (2) by passage of nitrogen into a borosilicate glass nebulizer which contained the thiol.
- Desired exposure concentrations of thiols were maintained in a glass chamber of approximately 18-liter capacity by varying the ratio of volume flow (liters/minute) of compressed air and compressed nitrogen.
- Prior to entering the chamber, the compressed air was scrubbed by passage through a fritted bubbler containing potassium dichromate in concentrated sulfuric acid, thence through a column of glass wool which was followed by a column of Drierite.
- From this it went into a mixing tube which received the thiol vapors by another inlet; the mixture then passed into the exposure chamber.

SAMPLING AND ANALYSIS OF EXPOSURE ATMOSPHERE
- During exposure periods the concentrations of thiols within the chamber were determined routinely by absorption of vapors in either iso-propyl alcohol or acetone containing an excess of silver nitrate and titrating the uncombined silver amperometrically according to the methods of Grimes, et al. (1955).
- Samples for analysis were collected in an Erlenmeyer flask containing an excess of silver nitrate of known normality (approximately 0.01 N) in 50 ml of acetone or isopropyl alcohol; the choice of solvent was determined by the thiol used and its solubility therein.
- After the thiol vapors had been metered through this solution, the resulting precipitate (silver mercaptide) and other contents were

quantitatively washed from the flask and the excess silver titrated amperometrically with standard dodecyl mercaptan (approximately 0.044 N).
- Accuracy of the sampling technique and analytical procedure as applied to this work was tested by vaporizing known amounts of thiols and was found to be within 2% of that calculated.

EXPERIMENTAL ANIMALS
- Five to ten rats per dose group, averaging 200 +/- 20 grams.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS: LC50 values by inhalation were calculated by the method of Miller and Tainter (1944) using logarithmic-probit graph paper.

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
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**Type** : LC50
**Species** : mouse
**Strain** : Swiss
**Sex** : male
**Number of animals** : 45
**Vehicle** :
**Exposure time** : 4 hour(s)
**Value** : = 28 ppm
**Method** : other
**Year** : 1957
**GLP** : no
**Test substance** : other TS

**Method** : Comparable to OECD 403 " Acute Inhalation Toxicity".

**Result** : TIME OF DEATH
Cumulative Mortality During and After Exposure

20 ppm: 0-4 hr = 0/10; 24 hr = 0/10; 48 hr = 0/10; 15 day = 0/10

31 ppm: 0-4 hr = 0/10; 24 hr = 0/10; 48 hr = 3/10; 15 day = 7/10*

41 ppm: 0-4 hr = 4/10; 24 hr = 7/10; 48 hr = 8/10; 15 day = 10/10*

52 ppm: 0-4 hr = 9/10; 24 hr = 10/10

79 ppm: 0-4 hr = 5/5 (2 hrs post exposure).

* 2 deaths from pulmonary infections - some pneumonia.

CLINICAL SIGNS : From paragraph comparing several thiols tested by inhalation:
- Maximal sublethal and lethal concentrations induced characteristic symptoms of toxicity, i.e. increased respiration and restlessness,

incoordinated movement and staggering gait, muscular weakness, partial skeletal muscle paralysis beginning in the hind limbs, light to severe cyanosis, tolerance of prone position, and mild to heavy sedation.
- Fatal Responses usually followed one of two patterns:
(1) animals exposed to maximal lethal concentrations died from respiratory arrest while in or shortly after removal from the chamber, and
(2) those animals exposed to minimal lethal concentrations died while in a semiconscious condition of long duration. - The aromatic thiols induced some lethargy and sedation which was quickly terminated upon exposure to normal atmosphere.
- Most of the thiols were irritating to the mucus membranes within approximately 15 minutes after exposure to high concentrations as evidenced by their rubbing of the eyes and nose, eye closure, occasional sneezing, watering of the eyes, and retracting of the head.
- Corneal opacities or cloudiness in the eyes often occurred in mice just prior to or after death from expousre to benzenethiol.

LC50 24 hour = 47 ppm (Confidence Limits 43.4 - 50.6 ppm)
LC50 48 hour = 35.5 ppm (Confidence Limits 32.4 - 38.6 ppm)
LC50 15 day = 28 ppm (Confidence Limits 24.8 - 31.2 ppm)

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** : Benzenethiol (phenyl mercaptan), highest purity Eastman Grade.

**Test substance** : DOSES
20 ppm
31 ppm
41 ppm
52 ppm
79 ppm

DOSE ADMINISTRATION
- Four hour exposure periods.
- The generation of thiol vapors was accomplished by either of two methods: (1) bubbling a stream of nitrogen gas (to prevent possible oxidation to sulfide) through a midget fritted-glass bubbler, which contained the liquid thiol, or (2) by passage of nitrogen into a borosilicate glass nebulizer which contained the thiol.
- Desired exposure concentrations of thiols were maintained in a glass chamber of approximately 18-liter capacity by varying the ratio of volume flow (liters/minute) of compressed air and compressed nitrogen.
- Prior to entering the chamber, the compressed air was scrubbed by passage through a fritted bubbler containing potassium dichromate in concentrated sulfuric acid, thence through a column of glass wool which was followed by a column of Drierite.
- From this it went into a mixing tube which received the thiol vapors by another inlet; the mixture then passed into the exposure chamber.

SAMPLING AND ANALYSIS OF EXPOSURE ATMOSPHERE
- During exposure periods the concentrations of thiols within the chamber were determined routinely by absorption of vapors in either iso-propyl alcohol or acetone containing an excess of silver nitrate and titrating the uncombined silver amperometrically according to the methods of Grimes, et al. (1955).
- Samples for analysis were collected in an Erlenmeyer flask containing an excess of silver nitrate of known normality (approximately 0.01 N) in 50 ml of acetone or isopropyl alcohol; the choice of solvent was determined by the thiol used and its solubility therein.
- After the thiol vapors had been metered through this solution, the

resulting precipitate (silver mercaptide) and other contents were quantitatively washed from the flask and the excess silver titrated amperometrically with standard dodecyl mercaptan (approximately 0.044 N).
- Accuracy of the sampling technique and analytical procedure as applied to this work was tested by vaporizing known amounts of thiols and was found to be within 2% of that calculated.

EXPERIMENTAL ANIMALS
- Ten mice (Swiss derived) per dose group, averaging 25 to 28 grams.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS: LC50 values by inhalation were calculated by the method of Miller and Tainter (1944) using logarithmic-probit graph paper.

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
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### 5.1.3 ACUTE DERMAL TOXICITY

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 35 |
| **Vehicle** | : | |
| **Value** | : | = 300 mg/kg bw |
| **Method** | : | other |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Method** : Comparable to OECD 402 " Acute Dermal Toxicity".

**Remark** : Toxicity data for a limited number of rabbits (3 rabbits per dose, doses of 67 mg/kg, 134 mg/kg, and 269 mg/kg) was also provided. Rabbits were dosed using the same method on a 6 x 10 cm area of the upper midback. The following results were obtained:

Cumulative Mortality Following Single Cutaneous Application

67 mg/kg: 0-8 Hours = 0/3; 24 Hours = 0/3; 48 Hours = 0/3; 72 Hours = 0/3

134 mg/kg: 0-8 Hours = 0/3; 24 Hours = 0/3; 48 Hours = 1/3; 72 Hours = 2/3

269 mg/kg: 0-8 Hours = 3/3 (All dead in 4 hrs).

Estimated LD50 = 134 mg/kg.

**Result** : TIME OF DEATH
Cumulative Mortality Following Single Cutaneous Application

134 mg/kg: 0-2 Hours = 0/5; 2-4 Hours = 0/5; 4-8 Hours = 0/5;
8-16 Hours = 0/5; 72 Hours = 1/5

213 mg/kg: 0-2 Hours = 0/5; 2-4 Hours = 0/5; 4-8 Hours = 0/5;
8-16 Hours = 1/5; 72 Hours = 1/5

269 mg/kg: 0-2 Hours = 0/10; 2-4 Hours = 1/10; 4-8 Hours = 1/10;
8-16 Hours = 1/10; 72 Hours = 2/10

339 mg/kg: 0-2 Hours = 2/5; 2-4 Hours = 3/5; 4-8 Hours = 4/5;
8-16 Hours = 4/5; 72 Hours = 4/5

427 mg/kg: 0-2 Hours = 2/5; 2-4 Hours = 4/5; 4-8 Hours = 4/5;
8-16 Hours = 4/5; 72 Hours = 4/5

538 mg/kg: 0-2 Hours = 4/5; 2-4 Hours = 4/5; 4-8 Hours = 5/5

Benzenethiol was classified as moderately toxic by this route.

CLINICAL SIGNS
- Rats exhibited irritative responses characterized by "ground-pawing" movements and frequent attempts to scratch and bite their backs.
- Rats often displayed tremors followed by a convulsion of short duration prior to respiratory depression and coma.
- Produced an inflammatory reaction of the skin a few hours after application. The redness usually disappeared within 24 to 48 hours.
- Autopsies made on animals dying from acute doses of thiols adminstered percutaneously usually did not show significant gross or microscopic tissue changes.

The LD50 = 300 mg/kg (confidence limits 236 - 384 mg/kg).

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** : DOSES
67 mg/kg (rabbits only -- see Remarks)
134 mg/kg
213 mg/kg
269 mg/kg
339 mg/kg
427 mg/kg
538 mg/kg

PERCUTANEOUS APPLICATION
- Cutaneous LD50 values for rats, five groups of five each and one group of 10, were calculated from mortality data obtained by single application of undiluted compounds (dosage levels in geometric progression) to a clipped area of the animals' backs.
- In this method areas of approximately 3 cm2 of the upper midbacks of rats were clipped as close to the skin as possible, care being taken to avoid abrasions and cuts.
- Animals were then placed in individual retainers and measured amounts of materials were delivered dropwise upon the clipped areas of the skin, exercising care in restricting the entire dosage to these areas.

EXPERIMENTAL ANIMALS
- Rats were used of the same stock and weight.

- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.

STATISTICS
LD50 values were calculated by the method of Weil (1952).

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Test substance** : Benzenethiol (phenyl mercaptan), highest purity Eastman Grade.

**Reliability** : (2) valid with restrictions
**Flag** : Critical study for SIDS endpoint
31.12.2003 (10)

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

| | | |
|---|---|---|
| **Type** | : | LD50 |
| **Species** | : | rat |
| **Strain** | : | Wistar |
| **Sex** | : | male |
| **Number of animals** | : | 25 |
| **Vehicle** | : | other: Ethanol as 5% v/v solution |
| **Route of admin.** | : | i.p. |
| **Exposure time** | : | unspecified |
| **Value** | : | = 9.8 mg/kg bw |
| **Method** | : | LD50 by i.p. route of administration |
| **Year** | : | 1957 |
| **GLP** | : | no |
| **Test substance** | : | other TS |

**Result** : TIME OF DEATH
Cumulative Mortality Following Administration
6.7 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 0/5; Day 15 = 0/5

13.5 mg/kg: Day 1 = 0/5; Day 2 = 0/5; Day 3 = 0/5; Day 5 = 0/5; Day 10 = 2/5; Day 15 = 2/5

27.0 mg/kg: Day 1 = 3/5; Day 2 = 3/5; Day 3 = 3/5; Day 5 = 5/5 (one dead 6 hrs past 5 days)

54.0 mg/kg: Day 1 = 5/5 (All dead 1 hr 10 mins)

108.0 mg/kg: Day 1 = 5/5 (All dead 1 hr 5 mins)

CLINICAL SIGNS : From paragraph comparing several thiols tested by injection:
- Compounds had property of being soporific, the degree ranging from mild stupor to heavy sedation. These conditions were slight for the aromatic thiols.
- The response of the thiol-injected rats was fairly uniform in that the symptomology of acute poisoning developed in the order of: restlessness, increased respiration, incoordination, muscular weakness, skeletal muscle

paralysis in most cases (starting with hind limbs), heavy to mild cyanosis, lethargy and/or sedation, respiratory depression followed by coma and death in cases of lethal doses.

The LD50 1 Day (ip) = 25.2 mg/kg (confidence limits 17.9 - 35.4 mg/kg).
The LD50 15 Day (ip) = 9.8 mg/kg (confidence limit 7.0 - 13.7 mg/kg).

**Source** : Toxicologic Studies on Organic Sulfur Compounds. 1. Acute Toxicity of some Aliphatic and Aromatic Thiols (Mercaptans) -- (Fairchild and Stokinger, 1958).

**Test condition** : DOSES
6.7 mg/kg
13.5 mg/kg
27.0 mg/kg
54.0 mg/kg
108.0 mg/kg

Dose ADMINISTRATION
- Doses per Time Period: Single intraperitoneal - Ethanol as 5% v/v solution.
- Groups of at least five Wistar-derived rats, each weighing on the average 200 +/- 20 grams were injected intraperitoneally at dosage levels differing by a factor of either 1.26 or 2.0 in a geometric series, according to Weil (1952).

EXPERIMENTAL ANIMALS
- Rats were used of the same stock and weight.
- Routine sacrifice of rodents was accomplished by separation of the cervical vertebrae.
- Other than those previously designated for early sacrifice, all animals were kept at least two weeks following the study.
- Most animals were held for observation for a month prior to being either destroyed or sacrificed for the study.
- Tissue specimens were submitted for pathologic examination after having first been examined grossly and preserved in either buffered formalin or Zenker's fixative.
STATISTICS
LD50 values were calculated by the method of Weil (1952).

POST DOSE OBSERVATION PERIOD: minimum of two weeks, possibly one month.

**Test substance** : Benzenethiol (phenyl mercaptan), highest purity Eastman Grade.

**Reliability** : (2) valid with restrictions
31.12.2003 (10) (33)

## 5.8 TOXICITY TO REPRODUCTION

**Type** : One generation study
**Species** : rat
**Sex** : male/female
**Strain** : Sprague-Dawley
**Route of admin.** : gavage
**Exposure period** :
**Frequency of treatment** : Daily
**Premating exposure period**

| | | |
|---|---|---|
| **Male** | : | 7 Days |
| **Female** | : | 7 Days |
| **Duration of test** | : | |
| **Doses** | : | 35 mg/kg/day (7 mg/ml); 18 mg/kg/day (3.6 mg/ml); 9 mg/kg/day (1.8 mg/ml) |
| **Control group** | : | yes, concurrent vehicle |
| **Method** | : | other |
| **Year** | : | 1996 |
| **GLP** | : | yes |
| **Test substance** | : | other TS |
| **Method** | : | Reproductive Assessment by Continuous Breeding (RACB) protocol. Comparable to OECD Guideline 415 "One-Generation Reproduction Toxicity Study." |
| **Result** | : | LOAEL males: = 9 mg/kg<br>LOAEL Females/fetus: = 35 mg/kg (reproductive)<br><br>REPRODUCTIVE TOXICANT:<br>Male: yes, slight, based on an increased incidence of inhibited spermiation in all treated F1 males, and decreased epidiymal sperm motility in the 18 and 35 mg/kg F0 male.<br>Female: yes (developmental) slight, based on decreased pup weights.<br><br>BODY WEIGHTS:<br>No major effects in the F0 or F1 litter data, However consistently decreased live pup weights at 35 mg/kg were observed in both the F0 and F1 generations. During the Task 2 continuous breeding phase, live pup weights were decreased by 4 and 5 % in the 9 and 35 mg/kg dose groups. It is unclear why the 9 mg/kg group was affected, no changes were observed at 18 mg/kg. During the Task 3 female crossover mating (naïve males mated with 35 mg/kg females), the live pup weight was decreased by 9%. No decreases in the live pup weight were noted during the Task 3 male crossover mating. During the final litter of Task 2, the live pup weight was decreased by 14-16% on PND 4 and 7 in the 35 mg/kg dose group with no differences observed on PND 1, 14, or 21. The live pup weight of the F2 generation was also decreased during Task 4: decreased by 9 and 12% in the 18 and 35 mg/kg dose groups respectively.<br>No differences were observed in adult female body weight for either the F0 or F1 generations, adult body weight of F0 and F1 35 mg/kg males were consistently decreased.<br><br>LIVER AND KIDNEY WEIGHTS (relative to body weight):<br>Liver and kidneys were enlarged in a treatment related fashion in both F0 and F1 animals.<br>At necropsy a treatment related increase in the incidence of enlarged, pale, soft, and/or pitted kidneys was observed in the F0 and F1 males.<br>Microscopic examination of the liver and kidneys from F0 and F1 animals revealed treatment-related hepatic lesions. Males were more affected than females.<br>Dose (mg/kg)/ % increase/ sex<br>F0 Liver<br>9, 18, 35 / 20%, 3%5, 50% / male<br>9, 18, 35 / 11%, 18%, 36% / females<br>F1 Liver<br>9, 18, 35 / 18%, 37%, 62% / male<br>9, 18, 35 / 14%, 17%, 43% / females<br>F0 Kidney<br>9, 18, 35 / 30%, 53%, 104% / male<br>9, 18, 35 / 8%, 5%, 20% / females |

F1 Kidney
9, 18, 35 / 52%, 67%, 163% / male
9, 18, 35 / 12%, 6%, 26% / females

SPERM PARAMETERS:
Subtle changes were observed in sperm parameters of both the F0 and F1 generations. Epididymal sperm motility was decreased by 6 and 5% in the 18 and 35 mg/kg F0 males. Epididymal sperm motility was slightly but not significantly decreased by 4% in the 35 mg/kg F1 males. Although not statistically significant, epididymal sperm velocity was slightly decreased in the low (6%), middle (8%), and high (6%) F0 dose groups and in the high (7%) F1 dose group.
The weight of the right testis was increased by 11, 19, and 14 % in the 9, 18, and 35 mg/kg F1 males. Inhibited spermiation of the stage VIII-X tubules was observed in the 9 (6/10), 18 (6/10), and 35 (9/10) mg/kg F1 males.

CONCLUSIONS:
Results of this study have demonstrated that thiophenol is a slight female/developmental toxicant in Sprague-Dawley rats when administered in corn oil at 35 mg/kg based on decreased live pup weight during the crossover mating. Thiophenol was also determined to be a slight male reproductive toxicant at = 9 mg/kg based on an increased incidence of inhibited spermiation in all treated F1 males, and decreased epididymal sperm motility in the 18 and 35 mg/kg F0 males. Thiophenol is not a selective reproductive toxicant, since reproductive changes were seen only concomitant with significant hepatic and renal toxicity. (author)

**Source** : National Toxicology Program, 1996.

**Test condition** : Species/Strain:Rat/ Sprague-Dawley

Route of Administration: Oral (gavage)
Doses/Concentration Level:
- 35 mg/kg/day (7 mg/ml)
- 18 mg/kg/day (3.6 mg/ml)
- 9 mg/kg/day (1.8 mg/ml)

Control Group and treatment: Yes, corn oil gavage

Frequency of Treatment: daily until the day before euthanasia

Premating exposure (male and female): 7 days

Statistical Methods:
- Data from Tasks 2, 3, and 4 were statistically analyzed by Analytical Sciences Inc. (Durham, North Carolina). Most hypotheses were tested using the nonparametric multiple comparisons procedure of Dunn (1964) or Shirley (1977), as modified by Williams (1986). Shirley's test was designed to detect treatment related differences when the response to treatment consistently increased (or decreased) with increasing dose. Although the test employed a smoothing alogrithm to adjust for dose-response inversions, Dunn's test was more appropriate if the departure from monotonicity was severe. Jonckheere's test (1954) was used to ascertain whether there was sufficient evidence of a dose-related response to apply Shirley's test. If the p-value from Jonckheere's test was less than 0.01, Shirley's test was used; otherwise, Dunn's test was applied.
- In the crossover mating trial (Task 3), the Kruskal-Wallis test (Kruskal-Wallis, 1952) was used to test equality of response among dose groups, while multiple comparison tests used the method of Dunn.
- For data expressed as a proportion, the Cochran-Armitage test (Armitage, 1971) was used to test for a dose-related trend, and pairwise comparisons

were performed using a chi-square test (Conover, 1971).
- A parametric analysis of covariance (Neter and Wasserman, 1974) was used to test overall equality in average pup weight, after adjustment for average litter size. Pairwise comparisons were performed using Dunnett's test (1955).
- Vaginal cytology data were analyzed using a multivariate analysis of variance (Morrison, 1976) to test for the simultaneous equality of measurements across dose levels. Before applying the test, an arcsine transformation was performed to bring the data into closer conformance with normality assumptions.
- All findings reported as "increased" or "decreased" were statistically significant as compared to the control group.

STUDY DESIGN:

Task 1: Dose range-finding phase (not conducted sufficient data was available to select dose)
Task 2: F0 generation continuous breeding
Task 3: F0 male and female crossover breeding with untreated animals (control and high dose groups)
Task 4: F1 fertility assessment

Test Animals:
- Animals were approximately 11 weeks of age at the initiation of dosing and the body weight range of the animals was:
--- Task 2: 288.2-423.5 g for males and 214.0-287.4 g for females.
--- Task 3: 342.2-426.5g naïve males, 229.5-270.6 g naïve females

Test Design (vehicle, dosing schedules, pre& post observation):
- Vehicle: corn oil
- Task 2, 3: 20 animals/sex/group

Mating Procedures:
- Task 2: Continuous Breeding Phase: Following seven days of premating exposure to thiophenol by oral gavage, the animals were housed as breeding pairs for 112 days (16 weeks). Litters produced during the cohabitation were counted and weighed by sex on PND 1 and then euthanized. At the end of 112 days, the pairs were separated with continued dosing. Any litters born (F1) after the continuous breeding phase were reared by the dam until weaning on PND 21. Selected weanlings were raised in same sex groups until 81 +/- 10 days of age. F1 animals were dosed, after weaning, with the same level their parents received. These F1 animals were used for assessment of second-generation reproductive toxicity.

- Task 3: Because decreased pup weights were seen during Task 2, a one week crossover mating trial was performed on the parental animals from the control and the high dose groups to determine the affected sex. Low- and mid-dose animals were maintained at the same dosing regimen until the control and high dose animals were euthanized and necropsied. After Task 3 crossover mating, F0 animals were necropsied and terminal body weights and organ weights were obtained, sperm were analyzed, and reproductive tissues were saved.

- Task 4: Assessment of F1 generation, conducted using offspring from all 4 dose groups. At 81 +/- 10 days, twenty control animals of each sex and 20 treated animals in each dose group were randomly assigned to breeding pairs, avoiding sibling mating, and cohabitated for seven days then separated. Offspring were counted and weighed by sex on PND 1. At necropsy terminal body weight and organ weights were obtained, sperm analyzed, and reproductive tissues saved in fixative.

| | | |
|---|---|---|
| **Test substance** | : | Thiophenol (CAS No. 108-98-5, R.O.W. Sciences ID No. 1003) purchased for Aldrich Chemical Company (St. Louis, Missouri) and provided by the NTP through Research Triangle Institute. 101% pure (estimated by high performance liquid chromatography) |
| **Reliability** | : | (1) valid without restriction |
| **Flag** | : | Critical study for SIDS endpoint |
| 02.01.2004 | | (3) (6) (7) (8) (12) (13) (17) (20) (21) (30) (36) |

## 5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

| | | |
|---|---|---|
| **Species** | : | rat |
| **Sex** | : | female |
| **Strain** | : | Sprague-Dawley |
| **Route of admin.** | : | gavage |
| **Exposure period** | : | Gestation Day 6 through 15 |
| **Frequency of treatment** | : | Daily |
| **Duration of test** | : | Approximately 27 days (including 7 day quarantine before mating) |
| **Doses** | : | 0, 20, 35, 50 mg/kg/day |
| **Control group** | : | yes, concurrent vehicle |
| **NOAEL Teratogen** | : | = 20 mg/kg bw |
| **LOAEL Maternal Toxicity** | : | = 20 mg/kg bw |
| **Method** | : | OECD Guide-line 414 "Teratogenicity" |
| **Year** | : | 1994 |
| **GLP** | : | yes |
| **Test substance** | : | other TS |

**Result** :

Results presented in the following format:
Dose in mg/kg/day / Target Concentration in mg/ml / Replicate 1 Pre-Exposure Concentration as % of target / Replicate 2 Pre-Exposure Concentration as % of target
0 / 0 / <DL / <DL
20 / 4 / 98 / 99
35 / 7 / 91 / 100
50 / 10 / 108 / 104
DL-Detectable limit

MATERNAL DATA:
- LOAEL: 20 mg/kg/day
- NOAEL: Could not be determined based upon the doses evaluated in this study
- Based upon minor, transient decrease in maternal weight gain and food consumption on GD 6 to 9 at 35 mg/kg/day.
- Decrease in body weight and weight gain, decrease in food consumption during treatment period occurred at high dose level of 50 mg/kg/day.

FETAL DATA:
- NOAEL: 20 mg/kg/day
- Based upon reduced female fetal body weight observed at 35 mg/kg/day.
- Developmental toxicity observed as increased preimplantation death, decreased litter size, decreased fetal body weight, and increasing incidence of external malformations occurred at high dose.

MORTALITY
- 4 deaths in 50 mg/kg/day group
- One death on GD 10, two on GD 12, and one on GD 15.

PREGNANCY RATE

20 mg/kg/day: 100% (25/25)
35 mg/kg/day: 96% (24/25)
50 mg/kg/day: 100% (25/25)
Control: 100% (25/25)

DURATION OF PREGNANCY: dams sacrificed PND 20 (before delivery)

BODY WEIGHT: Maternal body weight was decreased in the high dose group on GD 9, 12, 15, 18, and 20. Maternal weight change was decreased in all treatment groups on GD 6 to 9, and in the high dose group on GD 9 to 12, 6 to 15 (treatment period), 0 to 20 (gestation period) and for corrected maternal weight gain.

FOOD/WATER CONSUMPTION:
- Absolute maternal food consumption was decreased in all treatment groups on GD 6 to 9, and in the high dose group for GD 9 to 12, and 6 to 15. An increasing trend in absolute maternal food consumption was noted on GD 18 to 20. Relative maternal food consumption was reduced in all treatment groups on GD 6 to 9, and in the high dose group for GD 9 to 12, and 6 to 15. A significant increase in maternal food consumption was observed on GD 15-18, GD 18 to 20, and GD 15 to 20 in the high dose group.
- Absolute (g/day) maternal water consumption was increased in the high dose group on GD 12 to 15, 15 to 18, 18 to 20, 6 to 15, and 15 to 20. An increasing trend in absolute maternal water consumption was noted on GD 6 to 9 and 9 to 12. Relative maternal water consumption was increased in the high dose group compared to the controls at all intervals from the beginning of dosing through the remainder of the study.

CLINICAL SIGNS
-Rooting behavior observed in all groups during dosing period indicating an aversion to dosing formula. Showed dose-related increase and earlier onset with increasing dose.

ORGAN WEIGHTS (Significant change if $p < 0.05$)
- Decreased gravis uterine weight in the high dose group
- Increased relative and adjusted maternal liver weight in the high dose group
- Kidney weight unaffected

FETAL DATA:
No Effects Seen:
- Corpora lutea per litter
- Implantations per litter
- % preimplantation loss per litter
- % late fetal deaths per litter
- % fetuses with visceral malformations per litter
- % fetuses with skeletal malformations per litter
- % fetuses with variations per litter
- % litters with variations

Significantly Increased at High Dose (Significant change if $p < 0.05$):
- % reabsorptions per litter
- % litters with reabsorptions
- % nonlive implants( reabsorptions and late fetal deaths) per litter
- % litters with nonlive implants
- % fetuses per litter with external malformations
- % male fetuses per litter with any malformations

Decreased at High Dose (Significant change if $p < 0.05$):
- Number of live fetuses per litter
- Avg. fetal body weight per litter: Females more affected than males, and

weighed less in both the mid and high dose groups compared to controls.
- Avg. fetal body weight for males only decreased in high dose group.

**Source** : National Toxicology Program, 1994.

**Test condition** : DOSES (25 dams per group)
0 mg/kg/day
20 mg/kg/day
35 mg/kg/day
50 mg/kg/day

EXPOSURE PERIOD: Gestation Day 6 through 15

FREQUENCY OF TREATMENT: daily

CONTROL GROUP AND TREATMENT: 25 pregnant females dosed with corn oil

NUMBER OF ANIMALS: 25 pregnant females per dose

VEHICLE: Corn Oil

CLINICAL OBSERVATIONS: observed daily for clinical signs of toxicity

MATING PROCEDURES
- Individual breeding pairs were cohabited overnight
- Morning with sperm found in vaginal lavage designated as GD 0

PARAMETERS ASSESSED
Maternal
- Body weight GD 0, 3, 6 through 15, 18, and 20
- Food and water GD 0, 3, 6, 9, 12, 15, 18, and 20
- Clinical signs of toxicity
- Organ weights (Gravid uterine, liver, kidney)
- Implant status, Uteri with no visible implant sites stained with ammonium sulfide to detect early absorptions.
Fetal
- Weight, sex, and morphological development.

STATISTICS:
- General Linear Models (GLM) procedures were applied for the analyses of variance (ANOVA) of maternal and fetal parameters (SAS Institute, 1989a; 1989b; 1990a; 1990b; 1990c). Prior to GLM-ANOVA analysis, an arcsine-square root transformation was performed on all litter-derived percentage data to normalize the means (Snedecor and Cochran, 1967) and Bartlett's test for homogeneity of variance was performed on all data to be analyzed by ANOVA (Winer, 1962). GLM-ANOVA analysis determined the significance of dose-response relationships and the significance of dose effects, replicate effects and dose x replicate interactions. When ANOVA revealed a significant dose effect ($p<0.05$), Dunnett's Test (Dunnett, 1955; 1964) and Williams' Test (Williams, 1971; 1972) were used to compare treated to control groups. One-tailed tests were used for all pair-wise comparisons except maternal food and water consumption, , fetal body weight, and percent male fetuses/litter.
- Nominal scale measures were analyzed by a Chi-Square Test for Independence and by the Cochran-Armitage Test for linear trend on proportional data (Agresti, 1990; Armitage, 1955; Cochran, 1954; SAS Institute, 1992). When a Chi-Square test showed significant experiment-wise differences, a one-tailed Fisher's exact probability test was used for pair-wise comparisons of treatment and control groups.

**Test substance** : Phenylmercaptan (Thiophenol) CAS Number 108-98-5, >99% pure.

| | | |
|---|---|---|
| **Reliability** | : | (1) valid without restriction |
| **Flag** | : | Critical study for SIDS endpoint |
| 02.01.2004 | | (1) (2) (5) (8) (9) (18) (23) (24) (25) (26) (27) (28) (31) (34) (35) (37) |
| **Species** | : | rabbit |
| **Sex** | : | female |
| **Strain** | : | New Zealand white |
| **Route of admin.** | : | gavage |
| **Exposure period** | : | Gestational Day 6-19 |
| **Frequency of treatment** | : | Daily |
| **Duration of test** | : | 44 days (including 14 day quarantine period) |
| **Doses** | : | 0, 10, 30, 40, 50 mg/kg/day (50 mg/kg/day dose in first replicate only, excluded from final study) |
| **Control group** | : | yes, concurrent vehicle |
| **NOAEL Maternalt.** | : | = 10 mg/kg bw |
| **NOAEL Teratogen** | : | >= 40 mg/kg bw |
| **Method** | : | OECD Guide-line 414 "Teratogenicity" |
| **Year** | : | 1994 |
| **GLP** | : | yes |
| **Test substance** | : | other TS |

**Result** :

Results presented in the following format:
Dose in mg/kg/day / Target Concentration in mg/ml / Replicate 1 Concentration as % of target / Replicate 2 Concentration as % of target
0 / 0 / <DL / <DL
10 / 10 / 107 / 98
30 / 30 / 101 / 100
40 / 40 / * / 102
50 / 50 / 107 / **
DL-Detectable limit
* The 40 mg/kg/day dose was not included in the first replicate.
** 50 mg/kg group dropped from second replicate due to maternal toxicity. Replaced with 10 mg/kg group.

MATERNAL DATA:
- NOAEL: 10 mg/kg/day
- Toxic effects at 30 and 40 mg/kg/day were minor and transient so that the evidence of toxicity was equivocal.

FETAL DATA
- NOAEL: >/= 40 mg/kg/day
- LOAEL: could not be determined at the doses evaluated in this study
- 40 mg/kg/day did not adversely affect growth, viability, or morphological development of offspring.
- 50 mg/kg/day found to be excessively toxic, resulting in maternal mortality and morbidity.

MORTALITY: One doe in 10 mg/kg/day group died following dosing on GD 13, one doe in the 30 mg/kg/day group died following dosing on GD 6.

PREGNANCY RATE:
Control: 100%
10 mg/kg/day: 82%
30 mg/kg/day: 91%
40 mg/kg/day: 69%

Although pregnancy rate appeared to decline in the high dose group, all values fell within the historical control range for laboratory.

Number of Corpora Lutea/Doe, % Pre-implantation Loss, & Number of Implantations/Litter: comparable across all groups.

DURATION OF PREGNANCY: Pregnant does killed on GD 30

FOOD/WATER CONSUMPTION & BODY WEIGHT
- Food consumption marginally affected by treatment. In treated animals, relative food consumption was comparable to vehicle controls before dosing, but tended to be reduced during dosing. After dosing ended decreased food consumption was no longer evident.
- Decrease in food consumption translated into significant, albeit transient, reductions in maternal body weight gain on GD 12-15, the same period with the greatest reduction in food consumption.

ORGAN WEIGHTS: No adverse effects on maternal absolute or relative liver, right kidney, or gravis uterine weight.

FETAL DATA
Endpoints Examined, No Effects Seen:
- No. of reabsorptions/litter
- % late fetal deaths/litter
- % nonlive implants/litter
- No. live fetuses/litter, avg male and female body weight/litter
- Sex ratio
- External, visceral, or skeletal malformations

Effects Seen:
- Increase in the percent of females with variations per litter at 40 mg/kg/day for the study as a whole, or at 30 and 40 mg/kg/day for Replicate 2 alone.
- This increase in variations was mainly confined to the presence of extra or rudimentary lumbar ribs.

**Source** : National Toxicology Program, 1994.

**Test condition** : DOSES
10 mg/kg/day
20 mg/kg/day
30 mg/kg/day
40 mg/kg/day
50 mg/kg/day (first replicate only, excluded from final study)

EXPOSURE PERIOD: Gestational Day 6-19

FREQUENCY OF TREATMENT: Daily

TEST ANIMALS
- Age at Study Initiation: 5-6 months
- Number of Animals
-- Control: 24 does
-- 10, 20, 30, 50 mg/kg/day: 26 does
-- 40 mg/kg/day: 15 does

VEHICLE: corn oil

MATING PROCEDURES
- Injection of Pregnyl (chorionic gonadatropin, 0.1 ml/kg) prior to insemination.
- Females inseminated with undiluted ejaculate on day designated as Gestational Day (GD) 0.

PARAMETERS ASSESSED DURING STUDY:
Maternal:
- Clinical signs

- Food consumption
- Body weight on GD 0, 3, 6-19, 25, & 30
- Organ weights, liver, right kidney, intact uterus
- Ovarian corpora lutea
- Number of implant sites, uteri with no visible implantation sites stained with ammonium sulfide to detect early reabsorptions.

Fetal:
- Weight
- External morphological abnormalities
- Skeletal malformations

STATISTICS:
- General Linear Models (GLM) procedures were applied for the analyses of variance (ANOVA) of maternal and fetal parameters (SAS Institute, 1989a; 1989b; 1990a; 1990b; 1990c). Prior to GLM-ANOVA analysis, an arcsine-square root transformation was performed on all litter-derived percentage data to normalize the means (Snedecor and Cochran, 1967) and Bartlett's test for homogeneity of variance was performed on all data to be analyzed by ANOVA (Winer, 1962). GLM-ANOVA analysis determined the significance of dose-response relationships and the significance of dose effects, replicate effects and dose x replicate interactions. When ANOVA revealed a significant dose effect ($p<0.05$), Dunnett's Test (Dunnett, 1955; 1964) and Williams' Test (Williams, 1971; 1972) were used to compare treated to control groups. One-tailed tests were used for all pair-wise comparisons except maternal food consumption, maternal body and organ weights, maternal weight gains, fetal body weight, and percent male fetuses/litter.
- Nominal scale measures were analyzed by a Chi-Square Test for Independence and by the Cochran-Armitage Test for linear trend on proportional data (Agresti, 1990; Armitage, 1955; Cochran, 1954; SAS Institute, 1992). When a Chi-Square test showed significant experiment-wise differences, a one-tailed Fisher's exact probability test was used for pair-wise comparisons of treatment and control groups.

**Test substance** : Phenylmercaptan (Thiophenol) CAS Number 108-98-5, >99% pure.

**Reliability** : (1) valid without restriction
**Flag** : Critical study for SIDS endpoint
02.01.2004 (1) (2) (5) (8) (9) (19) (23) (24) (25) (26) (27) (28) (31) (34) (35) (37)

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## 7.1 END POINT SUMMARY

## 7.2 HAZARD SUMMARY

## 7.3 RISK ASSESSMENT